BIOLOGICS & BIOSIMILAR

May 2016
IPPOSI Outcome Report

Biologics & Biosimilars

Biologic medicines; Biosimilar medicines; Safety & efficacy of medicines; Patient perceptions; Budget impacts

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As more originator biologic medicines approach the end of their patent, and an increasing number of biosimilars reach the stage of approval, the issue of their safe and effective use is topical, as well as controversial. Although biosimilars have the promise of reduced drug expenditure, where these savings will re-appear is a legitimate question. Informed patients and patient representatives are crucial to addressing their introduction and possible adoption.

The IPPOSI breakfast meeting on Biologics and Biosimilars aimed to provide more clarity on what patients and prescribers should expect from this shift in the treatment paradigm. The meeting was attended by a wide range of stakeholders, with representatives from patient organisations, the scientific and medical communities, industry, as well as Government agencies and Departments.

A survey of patients and patient organisations (see: page 12) uncovered reasonable levels of awareness & understanding of biologic medicines, but there were low levels of awareness and little understanding of biosimilars among patients.

The survey also highlights how patients prioritise safety over effectiveness, how there is a clear need for understandable, patient-focused information - and critically, the importance of patient involvement in decision-making regarding switching.

Dr Derick Mitchell
IPPOSI Chief Executive
Joan O’Callaghan from the Health Products Regulatory Authority (HPRA) was there to provide the regulatory perspective and she gave a brief overview of the biosimilar approval process. She explained to attendees that manufacturers of biosimilars must prove that their agent has similar quality, efficacy and safety to the originator drug, with no clinically meaningful differences between the two.

Concerns remain around interchangeability, substitution, and switching with regard to biologics and biosimilars.

Ms O’Callaghan explained that there is a wide variation in international policies with regard to these matters. While Ireland’s generic substitution policy, as defined under the Health Act of 2013, excludes biosimilars, the HPRA is cognisant of issues with regard to interchangeability and switching, and has recently issued guidance on this topic.

The HPRA issued guidance in relation to use of biosimilars in 2015.

The HPRA position on interchangeability and switching is that if it is planned to change the medicine a patient receives from an originator to a biosimilar medicine or vice versa, the treating physician should be involved, she explained. This should involve a discussion between the prescriber/patient and also the prescriber/dispensing pharmacist. The Authority also urges ongoing engagement between prescribers, dispensers, and those with responsibility for procurement. O’Callaghan said there should also be meaningful stakeholder engagement in order to ensure both the optimal use of resources as well as ensuring the best patient outcomes. Switching back and forth is not recommended due to the paucity of data on the impact of this.

The Authority is currently involved in a Regulatory Science Ireland project on biosimilars, working adjacently with University College Cork and the Irish Pharmaceutical and Healthcare Association (IPHA). Ms O’Callaghan explained that this is focused on identifying practical considerations for health professionals; a prescriber survey has already been carried out to determine the knowledge, behaviours, and attitudes towards biologic medicines, particularly biosimilars. The goal is to develop appropriate training material and online resources for both prescribers and patients.
Local introduction
Introducing biosimilars in an Irish hospital

Professor Laurence Egan from NUI Galway discussed concerns regarding indication extrapolations for biosimilars, particularly within autoimmune conditions such as rheumatoid arthritis, psoriasis and inflammatory bowel disease (IBD).

A biosimilar of the anti-tumour necrosis factor (TNF) infliximab was approved by the European Medicines Agency in 2013, and Professor Egan outlined concerns, formally stated by the European Crohn's and Colitis Organisation in a position statement, and echoed by his own hospital, regarding extrapolation for biosimilar infliximab, with no published data on its use in IBD.

Galway University Hospital (GUH) carried out a study in 2014 which investigated whether the biosimilar infliximab could provide advantages for patients and/or the hospital. This looked at switching existing rheumatoid arthritis (RA) patients who were already on infliximab to the biosimilar, as well as newly-presenting patients starting biologic therapy. The study also aimed to explore the cost implications of adopting the biosimilar infliximab for patients at GUH. It was supported by a detailed policy on Biosimilar Medicines drawn up by the hospital.

All 40 RA patients agreed to switch to the biosimilar, and while consultants were not confident of its use in IBD, it was agreed to start new infliximab patients on the biosimilar for a trial period. “No new problems arose and they have continued on it since,” explained Professor Egan. No IBD patients switched from the originator drug. He said patients were given additional information, such as leaflets.

The study was broadly successful, although there were too few patients involved to detect any significant differences in efficacy or safety.

Biosimilar infliximab has been subsequently adopted by several other Irish hospitals, and at least one private health insurer has approved reimbursement for infliximab biosimilar.

Professor Egan concluded by stating that infliximab biosimilar usage continues to grow, and was successfully introduced at GUH albeit with a different approach for RA and IBD patients, based on the available clinical data. He emphasised the key role and autonomy of the prescribing consultants and the crucial requirement of a defined policy on biosimilar adoption.
Professor Bjorn Moum of Oslo University Hospital Ulleval discussed the Norwegian experience with biosimilars. He echoed Professor Egan by saying that biosimilar use has increased in Norway, and with this the resulting economic impact has been felt. The first biosimilar was approved in February 2014, and at that time the professor penned an editorial explaining his scepticism towards biosimilars, as well as urging their conservative use, and only under close monitoring. This scepticism is mirrored throughout Europe, with the positions of the respective medical societies being quite similar.

Professor Moum explained that societies are generally quite neutral regarding switching but have broadly negative views on indication extrapolation. Various patient advocacy groups have also published their positions, and are broadly neutral or positive regarding biosimilars but again have concerns when it comes to extrapolation.

“My experience with my patients is that they have been more sceptical than my colleagues, about starting, but especially about extrapolation and switching from a stable treatment.” He said the policy is to inform all patients in advance that they plan to switch therapies at their next visit. While most accept this, some initially refuse to do so, and he added that new patients are also quite sceptical. Professor Moum advised that a comprehensive discussion should take place between the prescriber and the patient.

He continued by saying that while efficacy does appear to be similar between biosimilars and originator medicines, concerns remain about safety due to lack of clinical data. He is involved in a study being carried out in Norway, which has the goal of determining the safety and efficacy of switching from the originator infliximab to the biosimilar, compared with continuation of treatment with the originator.

The NOR SWITCH study involves patients with RA, spondyloarthritis, psoriatic arthritis, Crohn’s disease, ulcerative colitis, and chronic plaque psoriasis.

All new IBD patients were given the infliximab biosimilar from May 2014, and in September 2015 all patients were switched from the originator to the biosimilar, he explained. Switching was carried out for medical reasons, such as loss of response or adverse effects, but if patients were stable on their biologic therapy they remained on it. The results of this study will be delivered at a major European gastroenterology meeting this autumn.

Professor Moum said that the gastroenterology unit at his hospital gives more than 300 infusions of biologics each month, and this had increased more than 50 per cent in the past two years. There are capacity issues, as well as cost implications for this. Switching to biosimilars had resulted in significant cost savings at the hospital, but he raised the question of who benefits from these savings; Professor Moum’s department successfully negotiated that some of the savings be used to improve the IBD service by funding additional staff at the unit, such as an additional consultant and an IBD specialist nurse.
Although the Infliximab biosimilar (Remsima)
market share is steadily increasing in Norway,
there has been no concomitant fall in the use
of other anti TNF therapies, as would have been
expected, the professor explained. Instead, the
use of biologics is increasing, and this is for a
variety of reasons. Patients are being prescribed
biologics much earlier in their disease course
than before in a bid to reverse the disease
course and prevent complications; patients are
also being given intensified doses, as well as
combinations of different biologics in more
difficult patients. In Norway, patients are not
being prevented access to biologics for
economic reasons, although this is happening in
other countries.

Professor Moum posed the question: If
switching to a cheaper biosimilar results in
more patients on biologics, who will take on
these costs? These include not only the cost of
the therapy, but also the associated costs such
equipment, facilities, and staff. The concern is
also there that if manufacturers of originator
therapies are forced to reduce their price
dramatically, this may affect funding for further
innovative therapies.

“If switching to a
geraper biosimilar
results in more patients
on biologics, who will
take on these costs?”

Professor Bjorn Moum

“Biosimilars are here to stay. So far they appear
safe and can save great resources but the
future is complex with more biosimilars
expected. ‘Biogenerics’ are also coming, as well
as ‘biobetters’ and ‘biosuperiors’, and eventually
the second generation biologics,” he concluded.

“Biosimilar use has
increased in Norway,
and with this the
resulting economic
impact has been felt.”

Professor Bjorn Moum
A wide-ranging and interactive panel discussion, chaired by IPPOSI Chief Executive Derick Mitchell, took place following the presentations. The three speakers were joined by Professor Michael Barry from the National Centre for Pharmacoeconomics and John Church, CEO of Arthritis Ireland.

Mr Church spoke about the potential impact of biosimilars from the patient perspective. He believed this would be limited, citing the current failure rates of available biologics. Although the increased use of biosimilars may have a cost impact, this will not immediately benefit the patient, he said.

“We are talking about biosimilars but you could actually have ‘biopatients’ – no two patients are the same. You might have two females with RA, the same age, etc. but neither may respond to anti-TNFs, or one may respond positively and the other not. So it’s not going to close the gap on unmet needs.”

Asked if patients were actually more sceptical than doctors in this area, John Church responded with “my interpretation of the survey results are that safety is number one over efficacy, because ultimately the patient fully trusts the doctor as long as it is safe. We openly encourage patients to actively communicate with the doctor on that, and Arthritis Ireland has produced twenty drug-specific patient information leaflets to be sent out to clinics. I’m not sure any other patient organisation is doing that”, he added.

Drugs with new and different modes of action are required, he said, referencing the significant investment Arthritis Ireland are making in terms of research into personalised medicine as it becomes clear that anti-TNF therapies are not suitable for everyone. He also echoed previous statements that any savings achieved by the use of biosimilars should stay within the particular disease area, and be used to improve the service by hiring more clinicians and nurse specialists, with the ultimate goal of decreasing waiting lists.

Professor Barry followed by saying the “volume of biologics is going up and up and up”; therefore the real issue is sustainability.

“We can’t keep doing what we are doing or people will lose out. It might not be rheumatology patients but someone will lose out as we will not be able to afford everything. The biosimilars do afford us a chance to impact on an unsustainable situation.”

In response to a question by Dr Mitchell on where the cost savings would be re-appropriated, Prof Barry stated that he is a firm believer in “incentives” and agreed that at least some of these savings should be put back into patient care.

Professor Egan commented that both clinicians and patients have attempted to limit the “excessive” use of biologics, citing concerns
about safety, uncertainty about the long term impact of biologics on the natural history of disease, as well as a “moral or ethical perspective where we need to be sure we are prescribing these medications cost effectively”.

He admitted the “expense is hard to justify”, but emphasised the impact of improved quality of life for patients.

“It’s being able to remain in work, it’s avoiding complicated surgeries, potentially avoiding patients going on long term sick leave and requiring welfare. The pricing and value for money when it comes to patients is very, very complex.”

When asked how could some of the non-clinical impacts be appropriately incorporated into drug assessments, Professor Barry acknowledged that there has been a “sophistication” in relation to the case put forward by industry when medicines are being assessed for reimbursement.

“It does include a quality of life, a wide range of costs and benefits. I think it’s fair to say that all those aspects are taken into consideration when you are doing the value for money. You could argue that about ten years ago that wasn’t happening but it certainly is now.”

He added, however, that anti-TNFs had been made available in Ireland before the routine assessment of therapies commenced, and suggested that perhaps it is time to assess them again, alongside the biosimilars.

The key role of the patient voice was asserted throughout the discussion, and Professor Barry stated that he reads many patient submissions that now accompany requests for reimbursement, and is impressed by their content.

“Through collaboration with patient groups such as yourselves (IPPOSI), patients do know what’s coming next, they know what assessments we are going to do and we value their input. Very often, the patients have more insight into it than the prescribers.”

Ms O’Callaghan reiterated the importance of pharmacovigilance in relation to the biosimilars; she said that the establishment of Irish patient registries would be an ideal way to achieve close monitoring and reassure when it comes to the biosimilars.

“If there is an Irish registry it will give more assurance to prescribers and to patients as well, knowing that the safety of these products is being closely watched. As well as that, pharmaceutical companies would have to submit updated safety data to the regulator once the product is authorised because there would be a re-evaluation of the benefit/risk profile of the medicine every so often.”

Ms O’Callaghan added that when the infliximab biosimilar was approved by the European Medicines Agency in 2013, their advice was for safety data to be included in patient registries. The HPRA endorses that approach, she emphasised.

Asked if we have learned anything for the introduction of the next biosimilars, Professor Egan said that “based on our experience with biosimilar infliximab so far, I would say it has been positive for both IBD patients and for physicians as well”. Bjorn Moum agreed. “I think we have learned a lot from the first monoclonal biosimilars and the next ones will come onto the market faster, as the amount of reluctance will be less. However he clarified that “At the moment, it is all about costs. For the future, we need to take into account the global costs, not just the medical ones. In IBD, two-thirds of costs are indirect (sick leave, disability etc.)”
Conclusion

Key findings from event and patient survey

- Awareness is growing about biosimilars among patients
- Biosimilars may provide benefit in terms of cost savings
- Concerns remain about switching and interchangeability
- Safety and efficacy data is limited
- Close follow-up is required if a patient is prescribed a biosimilar
- More biosimilars are due to be approved in coming years
- Hope that use of biosimilars does not impede innovative drug development
- Patient experience must inform value assessments

You can find videos, speaker presentations and pictures from the day by clicking this link.

The survey results are available in Annex I of this report, and can be downloaded from the webpage link above.
Appendix I
Survey Results

The charts that follow display the results of a survey undertaken to map the difficulties faced by patients in the adoption of biosimilars.

Method:
• 10 multiple choice questions (online survey)
• Conducted in parallel by IPPOSI and Arthritis Ireland

Target:
• IPPOSI Patient Organisation Members (42 responses, 21 organisations)
• Arthritis Ireland patient members – direct patient engagement (150 responses)

1. Please indicate if you are familiar with the following terms:

![Charts showing familiarity with terms among Arthritis Patients and Patient Organisations](chart1)

2. Do you know the difference between a biologic and a biosimilar?

![Charts showing knowledge of biologic and biosimilar differences among Arthritis Patients and Patient Organisations](chart2)
3. Do you know the difference between a biosimilar medicine and a generic medicine?

![Pie chart showing ARTHRITIS PATIENTS and PATIENT ORGANISATIONS responses.]

4. When a doctor is prescribing a biologic or biosimilar to a patient, what question do you think patients would ASK FIRST about that biologic/biosimilar?

![Pie chart showing ARTHRITIS PATIENTS and PATIENT ORGANISATIONS responses.]

5. Do patients have access to patient-friendly, easily understandable information about biologics?

![Pie chart showing ARTHRITIS PATIENTS and PATIENT ORGANISATIONS responses.]

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6. Do patients have access to patient-friendly, easily understandable information about biosimilars?

7. (part I) What information would you like to receive on biologics?

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<thead>
<tr>
<th>Arthritis Patients – Top 4 responses (68 responses in total)</th>
<th>Patient Organisations – Top 4 responses (30 responses in total)</th>
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<tr>
<td>Safety / side</td>
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<tr>
<td>Effectiveness</td>
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<tr>
<td>How they work?</td>
<td>How they work?</td>
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<td>My treatment / condition</td>
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7. (part II) What information would you like to receive on biosimilars?

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<th>Arthritis Patients – Top 4 responses (82 responses in total)</th>
<th>Patient Organisations – Top 4 responses (24 responses in total)</th>
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<tr>
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<tr>
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<td>What are they?</td>
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<tr>
<td>Safety / side effects</td>
<td>Effectiveness</td>
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<tr>
<td>Effectiveness</td>
<td>Any information at all</td>
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8. What are your preferred sources of patient information? (multiple answers accepted)
9. (part I) Are you familiar with the European Commission's 2013 Consensus Paper, 'what you need to know about biosimilar medicines'?

9. (part II) Are you familiar with The HPRA Guide to Biosimilars for Healthcare Professionals and Patients?

10. How important is patient involvement and consent in any decision by the prescriber to change from a current treatment to an alternative treatment?
Appendix II: Biographies

SPEAKERS

Joan O’Callaghan is a Researcher for Regulatory Science Ireland (RSI); RSI is a network of interested parties from Academia, Health Products Regulatory Authority (HPRA), Pharmaceutical Industry, Medical Devices Industry and Government Agencies. Joan graduated with Honours in Pharmacy from Trinity College Dublin (TCD). Upon completion of her degree she undertook her pre-registration training at St. James’s Hospital, Dublin. Subsequently Joan worked as a pharmacist in both the hospital and community settings. In 2008 Joan joined the HPRA as a Pharmaceutical Assessor. Joan is leading the HPRA in a RSI project investigating the public health impact of the increased use of biosimilars. She is currently undertaking a MSc. in Biopharmaceutical Science run through IT Sligo and the National Institute of Bioprocessing Research and Training (NIBRT).

Professor Laurence Egan was recruited in 2005 by NUI Galway and the Health Service Executive Western Region as Professor of Clinical Pharmacology/Consultant Clinical Pharmacist and Head of the Department of Pharmacology & Therapeutics. He graduated from University College Galway in 1990 (M.B., B.Ch., B.A.O.), and completed internship, house officer and registrar training, based at University College Hospital Galway. He received a Masters in Medical Science from UCG in 1994. From 1994 to 1999, at the Mayo Clinic in Rochester, Minnesota he completed further training in Internal Medicine, Clinical pharmacology & Gastroenterology. He is chair of the Drug and Therapeutics committee of Galway University Hospitals and he was appointed Editor-in-chief of the Journal of Crohn’s and Colitis in February 2014.

Professor Bjørn Moum obtained his Medical degree (MD) in 1981 from the University of Århus, Denmark. He trained in Internal Medicine and Gastroenterology in Hospital Østfold and Rikshospitalet and was board certified in 1991. He is Professor of Medicine and Gastroenterology at Oslo University Hospital with a research focus on clinical epidemiology, genetics and therapies in IBD, reflux disease of the oesophagus and endoscopy cancer palliation. His scientific work has resulted in author or co-authorship on more than 180 peer-reviewed papers. Bjørn was a Board member in the Norwegian Gastroenterology Association (1998-2011) and was President from 2004-2009. He is a personally-elected member of the International Organisation for IBD (IOIBD) and has been the National Representative Member of the European Crohn’s and Colitis Organisation (ECCO).

Dr. Derick Mitchell is the Chief Executive of IPPOSI; Derick has over eight years experience of management, advocacy, scientific communications and patient/public engagement, through previous positions at both European and national level. From 2011-2015, Derick was Communications Manager with the EU Joint Programme – Neurodegenerative Disease Research (JPND), before taking up the position as IPPOSI CEO. Derick graduated with a BSc. in Biotechnology from NUI Galway and has completed a PhD in Molecular Medicine from University College Dublin.

CHAIR
Professor Michael Barry MB, FRCP, PhD is a Consultant Clinical Pharmacologist and Head of the Department of Pharmacology & Therapeutics at the University of Dublin, Trinity College. He is the clinical director of the National Centre for Pharmacoeconomics which conducts pharmacoeconomic evaluations on medicines prior to reimbursement under the Community Drugs schemes in Ireland. He is Past-President (2010-2011) of the International Society for Pharmacoeconomics and Outcomes Research (ISPOR). He was a board member of the Health Information and Quality Authority (HIQA) and is a member of a number of National Committees on pricing and reimbursement of medicines. Prof. Barry chairs the New Drugs Committee and the Medication Safety Committee at St. James’s Hospital, Dublin. In 2013 he was appointed as Clinical Lead for the new HSE Medicines Management Programme.

John Church joined Arthritis Ireland as Chief Executive Officer in May 2005 after 16 years in the private sector. John has extensive experience in the commercial marketing arena, having held senior marketing and commercial management roles within the food and drink sector. John has successfully transformed Arthritis Ireland into a respected national charity. This was achieved through employing good solid commercial marketing strategies and brand positioning techniques. An impact led organisation, Arthritis Ireland is the first medical charity in Ireland to fund academic chairs in rheumatology through the medical schools. A science graduate of University College Dublin, he holds a marketing degree from the University of Leuven in Belgium and a diploma in direct marketing from Kingston University, London.