Current Guidelines on the use of Biosimilars

Harbans Dhillon B Pharm
Past President of ISOPP
Past Deputy Director of University Malaya Medical Centre, Kuala Lumpur Malaysia
Disclosure

Speakers bureau - Pfizer
Learning objectives:

- Uptake of biosimilars
- Countries with biosimilar guidelines
- Various guidelines available for biosimilars
  - WHO guidelines
  - EMA Guidelines
  - British Oncology Pharmacy Association (BOPA)
  - ESMO
Uptake of Biosimilars

- With the emergence of biosimilars worldwide, guidelines are much needed to ensure proper usage.
- The uptake of biosimilars & potential for cost savings depends on several factors & strategies that can vary between different countries & continents.
- These include:
  - patent protection
  - regulatory requirements
  - health technology assessment (HTA)
  - reimbursement processes
  - procurement & tendering processes
  - positions on interchangeability, substitution & switching.
World map showing countries that have biosimilar guidelines

- Include USA, Canada, Europe, India, Australia, Japan, South Korea, South Africa, China, Brazil, Mexico, Argentina, Peru, Colombia, Venezuela, Chile, Cuba, Singapore, Malaysia, Thailand, Saudi Arabia, Egypt, Uganda, Turkey
- Countries which are on the verge of publishing their biosimilar guidelines Russia
- Countries which do not have any biosimilar guidelines (white).

Figure adapted from Scheinberg MA, Kay J. *Nat Rev Rheumatol*. 2012;8:430-436.
**WHO Guidelines**

- Provide globally acceptable principles for licensing biotherapeutic products that are claimed to be similar to, of assured quality, safety & efficacy that have been licensed based on a full licensing dossier.

- Can be adopted as a whole, or partially, by NRAs worldwide.

- Or used as a basis for establishing national regulatory frameworks for licensure of these products.

- Many countries based their regulatory requirements on the principles established by these guidelines.
WHO guidelines

- To harmonize regulations worldwide, WHO issued guidelines following very similar principles to those of European Medicines Agency (EMA).
- Many developed countries have rigorous regulatory processes that ensure comparability of biosimilars with their reference products.
- Although regulations vary substantially across countries, many countries are striving toward harmonization of accepted criteria by EMA, US FDA & WHO.
- However, there is still a lack of a uniform approach to the regulatory approval & in some countries, synthetic copies of brand compounds have been approved without comparative clinical studies with the innovator.
Regulations in EU

• First region to have pioneered & set up a legal framework (EMA)
• Concept of biosimilar adopted in EU legislation in 2004
• First biosimilar medicine approved by EU in 2006
• Acceptance & demand among payers & public are increasing
• Biosimilar versions of more than 40 insulins are currently under development in the EU
• Global biosimilars sales in 2013 reached only $1.3 billion, but by 2020 biosimilars penetration is expected to have delivered from $11 billion to $33 billion in savings across the EU
• EU contribution to the regulation of biosimilars worldwide.
European Medicines Agency

- Has overarching biosimilar guidelines
- Outlines quality, non-clinical & clinical data requirements specific to biosimilar drugs
- Supplemented by eight product class–specific guidelines (e.g. a guideline for biological medicinal products containing monoclonal antibodies) & other guidelines relevant for biosimilar evaluation including immunogenicity & comparability guidelines
- In addition, EMA & European Commission have published an information guide for health care professionals
- Summarizes the science & regulation underpinning the use of biosimilar medicines.
European Medicines Agency
Guideline on similar biological medicinal products:
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■ Regulatory framework and scope
■ Legal basis and relevant guidelines
■ Application of the biosimilar approach
■ Choice of reference product
■ Principles of establishing biosimilarity
Biosimilars in the EU – information guide for healthcare professionals

- Biological medicines – overview, definitions & features
- Why biosimilars are not considered generic medicines
- Development & approval of biosimilars in the EU
- Safety of biosimilars
- Data included in the prescribing information & EMA assessment reports for biosimilars
- Implications of the availability of biosimilars
- Interchangeability, switching & substitution: EMA & Member States’ responsibilities
Guidelines on implementation of biosimilar MABs - BOPA

• Granulocyte colony stimulating factors (GCSFs) & erythropoetins (EPOs) introduced as supportive therapies for cancer patients

• First biosimilar MAB widely introduced in the UK were biosimilars of infliximab

• In 2017 IV biosimilar rituximab was introduced for haematological malignancies followed by IV biosimilar trastuzumab for breast cancers

• Has a position statement on implementation of biosimilar monoclonal antibodies.
Role of Oncology Pharmacist BOPA

Oncology pharmacists will contribute to:

• Medicine optimisation of biosimilars
• Supporting commissioning of biosimilars
• Ensuring local physicians are engaged & informed
• Ensuring patients are appropriately educated & informed
• Ensuring any pharmacovigilance processes are followed e.g. monitoring
• Managing process of switching initially & in future
• Ensuring optimisation of prescribing – e-prescribing.
Factors Affecting Health Care Provider Knowledge and Acceptance of Biosimilar Medicines: A Systematic Review

Emily Leonard, PharmD Candidate; Michael Wascovich, PharmD, MBA; Sonia Oskouei, PharmD; Paula Gurz, MBA; and Delesha Carpenter, PhD, MSPH

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Findings

- Clinicians in the US & Europe are cautious about biosimilar use & do not predominantly support the use of biosimilars as safe & effective treatment options in patients already receiving bio-originator therapy
- Provider hesitancies deter biosimilar prescribing & use
- Education can help to increase prescriber comfort & familiarity with biosimilar medicines, inspire prescribing changes & ultimately drive biosimilar use
- However, biosimilar-specific education remains a relatively neglected area of emphasis in the published literature
- This review identifies several topics that clinician-tailored biosimilar education should address to alleviate existing misunderstandings & bridge knowledge gaps altogether.
Findings

- Major areas of focus reviewing concepts of immunogenicity, extrapolation & interchangeability
- Future research should explore different health care provider types in greater detail & evaluate practitioners’ engagements with patients to ensure that providers can effectively communicate with their patients about biosimilars as a treatment option
- A mixed-methods study including exploratory semi-structured qualitative interviews & a quantitative survey assessment of US &/or European clinicians should be conducted to assess perceived biosimilar educational needs.
Recommendations

• Whilst guidelines exist, there is no incorporation of these guidelines at national levels in some countries

• Establish working groups to assist regulatory authorities in their efforts to develop & introduce biosimilars into respective countries

• There is an urgent need for enhanced training of regulatory authorities on how to evaluate biosimilars

• PIL prepared on a national level to provide uniform information for patients & caregivers

• Education programs on biosimilars of healthcare professionals are needed to create trust in these products.
Safety of biosimilars (pharmacovigilance)

- Once a biosimilar is on the market, continuous monitoring is required to ensure its safety & efficacy.
- Some side effects are only seen after prolonged exposure or a large number of patients are treated, additional pharmacovigilance & phase IV studies are essential.

Tabernero J, et al. ESMO Open 2016;1:e000142. doi:10.1136/esmoopen-2016-000142
Challenges ahead

- Cross-over trials would be needed to prove interchangeability of a drug
- Pharmacists need more information to the type & amount of clinical trial data needed for biosimilar approval & technical information on comparability exercises
- A notable number of physicians & patients have important knowledge gaps
- Education of all interested parties, administrators, policy makers, physicians, pharmacists, nurses, patients, payers
- Continued data collection.
ISOPP’s take on Biosimilars

• A Biosimilar Task Force has been set up
• Aims to provide the global oncology pharmacy community with guidance to support decisions around biosimilar use
• Sent out a biosimilars survey to members (needs & implementation)
• Working on a global position paper currently to provide the global oncology pharmacy community with guidance
• ISOPP believes that education regarding use of biosimilars is paramount to their safe & effective use
• Organizing a biosimilars interactive workshop at ISOPP 2019 symposium in London.
Biosimilars – a necessary opportunity

- Biosimilars present a necessary opportunity for physicians, patients & healthcare systems
- If properly developed clinically, manufactured to the correct standards & used appropriately, they can positively impact the financial sustainability of healthcare systems globally.

Tabernero J, et al. ESMO Open 2016;1:e000142. doi:10.1136/esmoopen-2016-000142
In Conclusion….

- Statement suggests “with potential savings, a rapidly increasing range of biologic products & well-informed healthcare professionals & patients, biosimilars represent one of the ways forward to obtaining sustainability”. *Position paper by ESMO*

- With growing financial constraints on healthcare systems & impending patent expiry on major biologic therapies used in oncology, biosimilars offer an important opportunity to provide a high quality & clinically effective medications at reduced cost

- The end goal is to ensure the patient receives the best, safe, efficacious & *affordable* treatment.
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