The Need for Biosimilars in the USA –obstacles and solutions

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Dr Nigel Rulewski MB, BS. DRCOG. DCH.
VP and Head of Global Biosimilar Unit
Quintiles



Biosimilars Knowledge Connect

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Agenda

- Biologics: why are they so important?
- Biologics: why is the current situation unsustainable?
- Consequences for patients?
- Obstacles to developing biosimilars in the USA
- What is being done to improve patient and investigator awareness?

Biologics: why are they so important?

Biologics have had a profound impact in healthcare over the past 20 years

- **Herceptin® in HER-2+ breast cancer**
  Disease recurrences halved; mortality reduced by a third[1]
- **Rituxan® in non-Hodgkin's lymphoma**
  New standard of care, increased survival[2]
- **Benlysta® in lupus**
  First treatment advance in 50 years[3]
- **Anti-TNF-αs in RA and inflammatory bowel disease**
  Revolutionized care: sustained remissions, reduced need for surgery[4,5]
- **β-interferons in multiple sclerosis**
  First disease-modifying therapy: fewer relapses and disability slowed[6,7]
- **Targeted biologic therapies in rheumatoid arthritis**
  Reduction in deformity; remission a realistic goal[8,9]

1. Duffy 2013; 2. Griffin & Morley 2013; 3. Mosak & Furie 2013; 4. Ahluwalia 2012;
5. Ferrante *et al*. 2009; 6. Derwenskus 2011; 7. Bell *et al.* 2011; 8. Scheinberg & Kay 2012;
9. Horton & Emery 2012

Seven of the world's top ten best-selling drugs are biologics

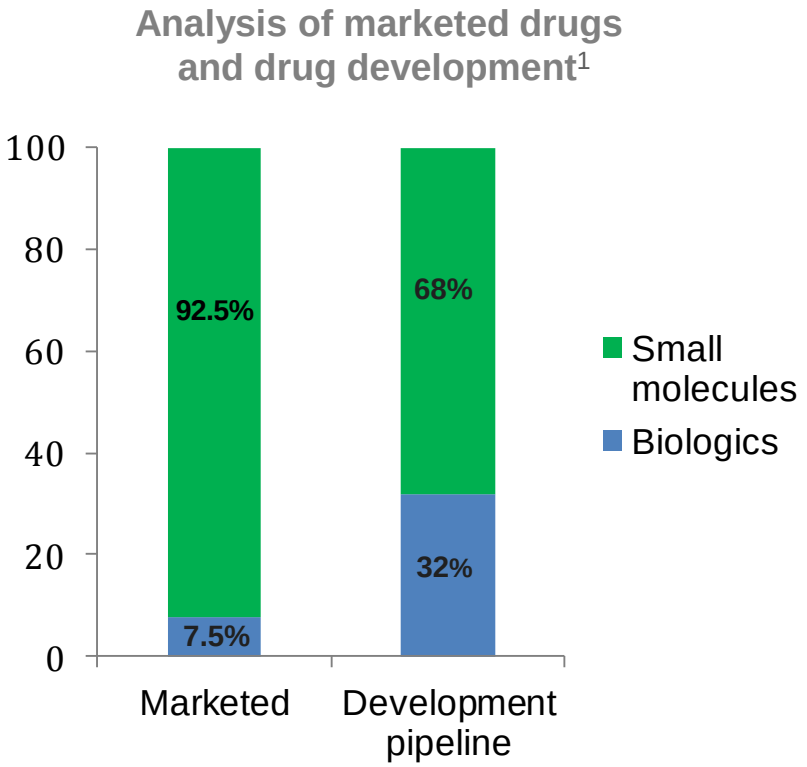
Ranked according to global sales by US dollars (2013 figures)[1]

1. Humira® (adalimumab)
2. Remicade® (infliximab)
3. Rituxan®/MabThera® (rituximab)
4. Advair®/Seretide® (fluticasone/salmeterol combination)
5. Enbrel® (etanercept)
6. Lantus® (insulin glargine)
7. Avastin® (bevacizumab)
8. Herceptin® (trastuzumab)
9. Crestor® (rosuvastatin)
10. Abilify® (aripiprazole)

1. *Genetic Engineering & Biotechnology News* 2014

Growth of biologics is increasing exponentially

- Almost a third of pharmaceutical products now in development globally are biologics[1]
  - › >20% forecasted growth each year[1]
  - › >50% of all new drug approvals by 2015; >70% by 2025[2]
- The demand for biologics will only increase
  - › Continued population growth
  - › Aging population



1. Simoens 2011; 2. Berkowitz *et al.* 2012.

Biologics: why is the current situation unsustainable?

Biologics are **prohibitively** expensive

Drug name	Indication(s)	Annual cost ($) per patient
Enbrel®	Rheumatoid arthritis, psoriatic arthritis, ankylosing spondylitis	15,345[1]
Remicade®	As above plus Crohn's disease, ulcerative colitis, and psoriasis	24,018[1]
Benlysta®	Lupus	35,000[2]
Herceptin®	Breast cancer	70,000[3]
Cerezyme®	Gaucher's disease	200,000[4]

2012 figures. Based on a reasonable course of therapy for the given indication(s).

Case studies

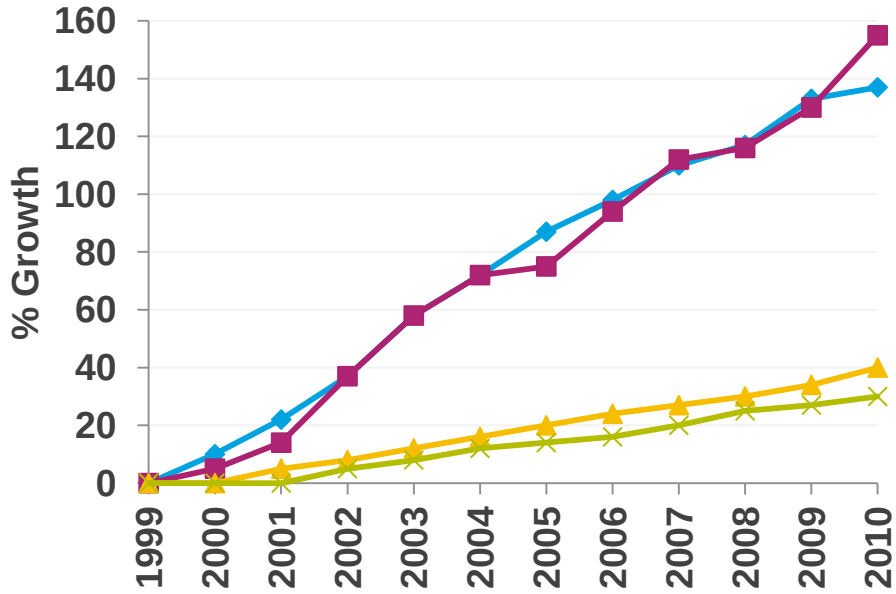
- Median survival greatly increased over the past decade with addition of cetuximab to standard chemotherapy for metastatic colorectal **cancer**[5,6]
- However, the average cost of 8 weeks' therapy rose from $9,381 to $30,675
- Cost of Gleevec has increased since launch from $24,000 to $90,000 per year

1. Bonafede *et al.* 2012; 2.*The Pharma Letter* 2012; 3. *Medical News Today* 2012; 4. Forbes 2012; 5. Schrag 2004; 6. Heinemann *et al.* 2013

In Particular, Oncology Care And Drugs Are A Significant Driver Of Increased Costs

"The twin driver of increasing cancer prevalence as populations age and cancer medicine costs rising faster than inflation places oncology as the most significant single cost problem"

Yearly Growth In Key US Health and Household Fiscal Metrics



US, 2010: - Direct medical spending on cancer: $104B – *an increase of 222% over 20 years*

Why is the current situation unsustainable

- Present expenditure on health care in the US accounts for 20% of GDP, biologics contribute significantly to this situation
- US spend $80 billion on biologics in 2013
- Biologics are, on average 20 times as expensive as small molecule drugs,
- Biologics are increasing their share of the total pharmaceutical market
- NICE has rejected several applications to fund cutting-edge cancer drugs on the NHS
- In April 2014, revolutionary breast cancer drug Kadcyla® was rejected despite a 5.8 month improvement in survival benefit.
- The Herceptin®-based drug can prolong lives by nearly 6 months but costs $9800 per month or $94,000 for typical course of treatment
- Patients are not getting access to these new products

Consequences for Patients

Potential impact of Biosimilars in the US:

- As no biosimilars are presently approved in the US we look to EU for data:
- on average biosimilars are 30% cheaper than the innovator product
- 2007 -2020 savings are estimated to be $11.8-33.4 billion (8 main EU territories)
- US estimates that 11 top products as biosimilars would save $250 billion (2014-2014)

Introduction of biosimilars in Europe has led to significant cost savings

- Developing a biosimilar costs approximately 100 times more than a generic so discount offered can't match[1]
- However, savings are still significant given high cost of biologics

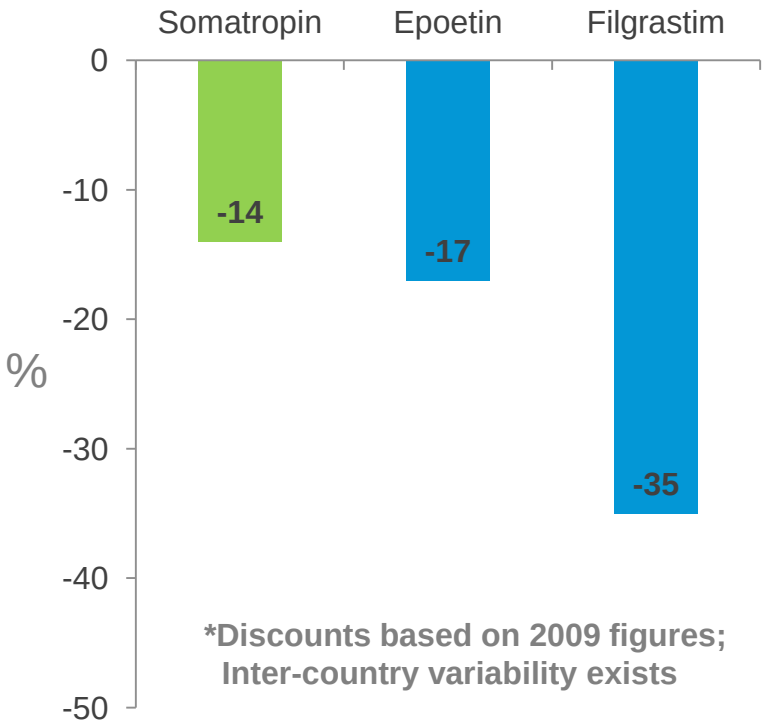
EU

Typical discounts of 10–35%,[2] with forecasted savings of between €11.8 and €33.4 billion in eight EU countries by 2020[3]

USA

Expected to save consumers $25 billion/ decade[4] and Medicare $9–12 billion/ decade[5]

Mean discount (biosimilar vs originator) across EU countries (n=24)*[2]



1. Federal Trade Commission 2009; 2. Rovira *et al.* 2011; 3. Haustein *et al.* 2013; 4. Hirsch & Lyman 2011; 5. Quereshi *et al.* 2013

The FDA has approved a few "follow-on proteins" of simpler biologics[1]

INN	Follow-on protein	Company	Approval
Glucagon (recombinant)	GlucaGen	Novo Nordisk	1998
Hyaluronidase	Amphadase	Amphastar	2004
	Hylenex	Baxter	2005
	Hydase	PrimaPharm	2005
Calcitonin salmon	Fortical	Unigene/ Upsher-Smith	2005
Somatropin	Omnitrope	Sandoz	2006

These "follow-on proteins" are generally not termed biosimilars as they were approved via the 505(b)(2) pathway

By August 2014, no biosimilars had yet been approved via the new 351(k) pathway, although two applications had been accepted

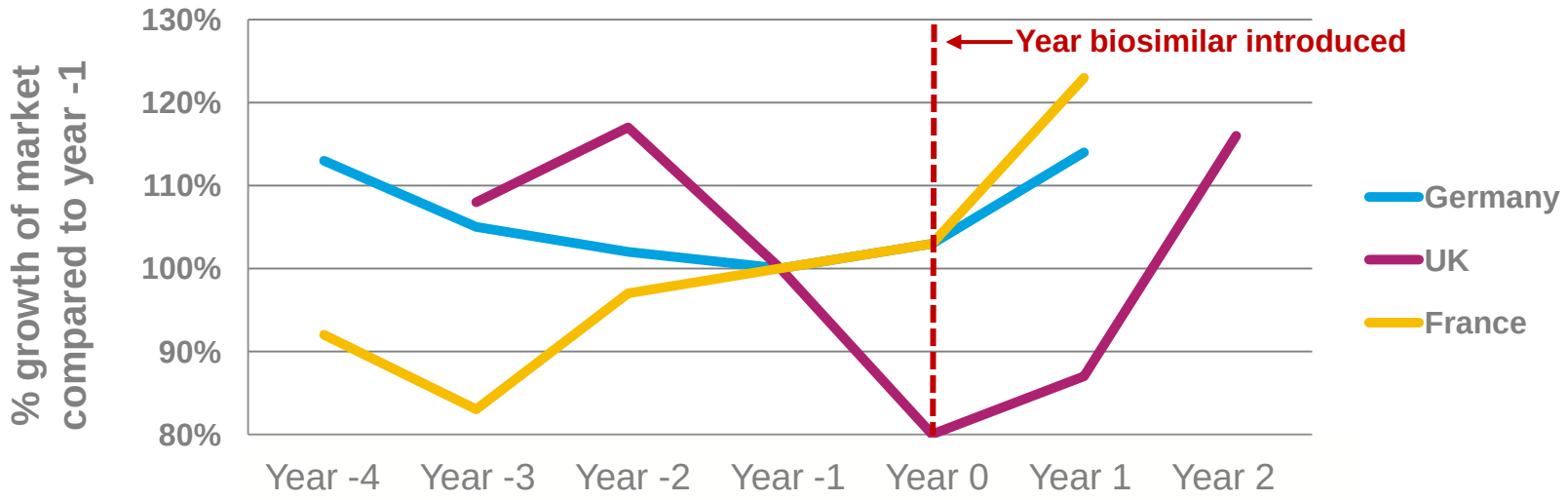
1. Woodcock *et al.* 2007

Biosimilars have improved standards of care

Case study – filgrastim (G-CSF) biosimilar in the UK[1]

UK clinical guidelines recommend filgrastim for prophylaxis of febrile neutropenia. However, use was restricted until after the condition had developed owing to cost. Once an affordable biosimilar of filgrastim was introduced, clinical practice shifted towards recommended prophylactic use.

Filgrastim (G-CSF) market share before and after the introduction of a biosimilar in Europe



Source: Adapted from IMS Health, Shaping the Biosimilars Opportunity, December 2011.

1. McCamish & Woollett 2012

What impact could biosimilars have in key therapy areas?

Biosimilars could put modern cancer biologics within reach of many more patients worldwide

- The USA, together with the five largest EU countries, account for 65% of the total oncology market[1]
- Spending for cancer has risen 222% in the USA over the past 20 years[2]
- Many new generation biologics for cancer cost $100,000 per patient per year[2]
- Between 2011 and 2014, the UK's NICE rejected eight consecutive applications for new breast cancer biologics[3]



NICE = National Institute for Health and Care Excellence
1. IMS Health 2012; 2. Cornes 2012; 3. FiercePharma 2014

Biosimilars could broaden access to insulin

- Insulin is included on the WHO's Essential Medicines List, although global availability is inconsistent[1]
- >80% of the world's diabetes population live in low- and middle-income countries, although 70% of insulin is used in developed countries[1]
- Patients may have to self-fund a high proportion of the cost of their medicines, up to 40–60% in Latin America[1]
- Yearly cost of insulin for type 1 diabetes may exceed a family's total annual income1. For example, in Malawi, one month's supply amounts to ~20 days' wages[2]
- In poorer countries, patients under-dose insulin in order to conserve supplies[3]



1. International Diabetes Federation; 2. Mendis *et al.* 2007; 3. Gill *et al.* 2011

Biosimilars could make use of biologics more routine in rheumatoid arthritis

- Use of rituximab in rheumatoid arthritis (often a crippling disease) has made remission a more realistic goal, but at a high cost

Drug	Course	NHS cost (UK)
Methotrexate (DMARD)	20 mg once weekly for 4 weeks	£2.14
Rituximab (biologic DMARD)	2 x 1000 mg IV infusions	£3,492.00

- In >50% of European countries, annual cost of a biologic DMARD can exceed the per capita GDP by as much as 11 times[1]
- Thus almost 40% of the total European population has severely restricted access to biologic DMARDs[1]
- In developing nations, where healthcare focuses on fatal diseases, access to biologic DMARDs can be almost unheard of[2]



DMARD = disease-modifying anti-rheumatic drug; GDP = gross domestic product

1. Putrik 2014; 2. Osiri & Maetzel 2010

Consequences for Patients in US

Apart from limiting access to new products, serious illness results in **Bankruptcy!**

- 1981- 8% of bankruptcy were due to serious illness
- 2001 – serious illness accounted for 50% of bankruptcy
- 2008- number had risen to 61%
- One in five families in the US use up their life savings paying for treatment
- Vast majority had insurance!
- Insurance premiums have more than doubled since 1999
- Most insurance programs have a 20% co-pay
- Patients need Biosimilars even in the US!

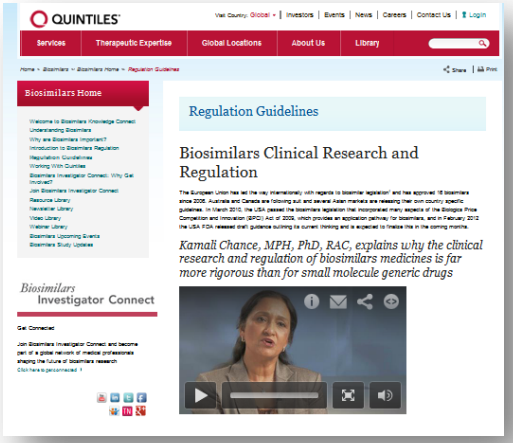
Obstacles to US development of Biosimilars

Obstacles to Biosimilar Development

- Lack of investigator interest:
- Prefer to work with NCE's and more innovative products
- Lack or awareness, understanding about biosimilars
- Some taking a 'wait and see' approach due to concerns about biosimilar safety
- 40% of potential investigators in the US have none, or limited knowledge of biosimilars
- In the EU, 20-30% of investigators are still unaware of biosimilars
- Lack of awareness of potential price reductions
- Lack of awareness of financial benefits to patients participating in biosimilar trials

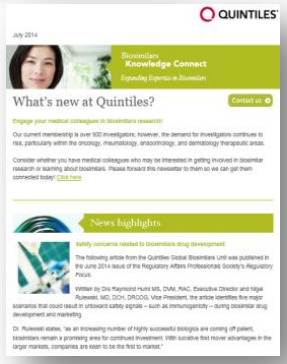
What is being done to improve investigator and patient awareness of biosimilar development programs

Website: Biosimilars Knowledge Connect





Regional guides to biosimilars



Quarterly newsletters

- Investigators are invited to register their interest in working with Quintiles via our website
- Educational resources can be accessed via our Biosimilars Library
  - Quarterly newsletters
  - Investigator and industry perspectives
  - Regional guides to biosimilars
  - Educational programs

Why should YOU participate in biosimilar research?

You could help to

- Provide your patients with **immediate access to biologics** and comprehensive care at no cost by means of clinical trial participation
- Improve **access** to vital biologics within your country and around the world once approved
- Ensure **high-quality clinical testing**, thus optimizing patient safety
- Collect **clinical data** on local populations
- Further the **field of biosimilars** within your country:
  - Publish findings of your research
  - Influence decisions of local payers and medical colleagues

Biosimilar trials need to demonstrate similarity, not patient benefit

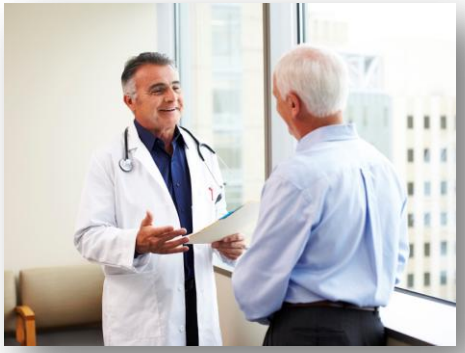
- The focus is **NOT** to establish patient benefit, as this has already been carried out for the originator[1]
  - › Instead, the objective is to demonstrate **high similarity to the already clinically proven originator**[1]
  - › Biosimilars are licensed on the basis of a reduced and less costly data package by building on the safety and efficacy experience of the originator[1]

It is not scientifically necessary or beneficial to repeat the entire development program of the originator[2,3]

1. Weise *et al.* 2012; 2. Kozlowski *et al.* 2011; 3. Noaiseh & Moreland 2013

Why should YOUR PATIENTS participate in biosimilar research?

- Educate your patients about the benefits of participating in a biosimilar trial, compared with one for a novel drug
  - Access to approved biologics, or their candidate biosimilars, at no cost (or earlier access than allowed by insurer guidelines)
  - Active medication with no risk of placebo
  - Reduced risk of treatment failure because the originator is known to be effective at the dose and frequency used in the clinical trial
- Consider use of recruitment tools to help explain
  - "Biosimilars" and how they differ from generics
  - Previous testing to demonstrate similarity to the originator
  - The contribution of biosimilars to improving patient access to biologics once approved



Summary

- The rising cost of biologic products places a significant burden on the US economy. Biosimilars have the potential to significantly reduce this burden
- Even patients with insurance, high co-pays place a significant burden on patients and their families
- High costs limits patient access
- Participating in clinical development programs for biosimilars can significantly reduce the financial burden on patients, not just for medications but for the overall health care costs
- Physicians, by participating in biosimilar development programs can offer biologic treatments with the need for insurance company approval and ensure patients have earlier access to these medications.
- Continuing education programs for both patients and physicians are striving to make these advantages better known