E-Conference

Valor em Saúde

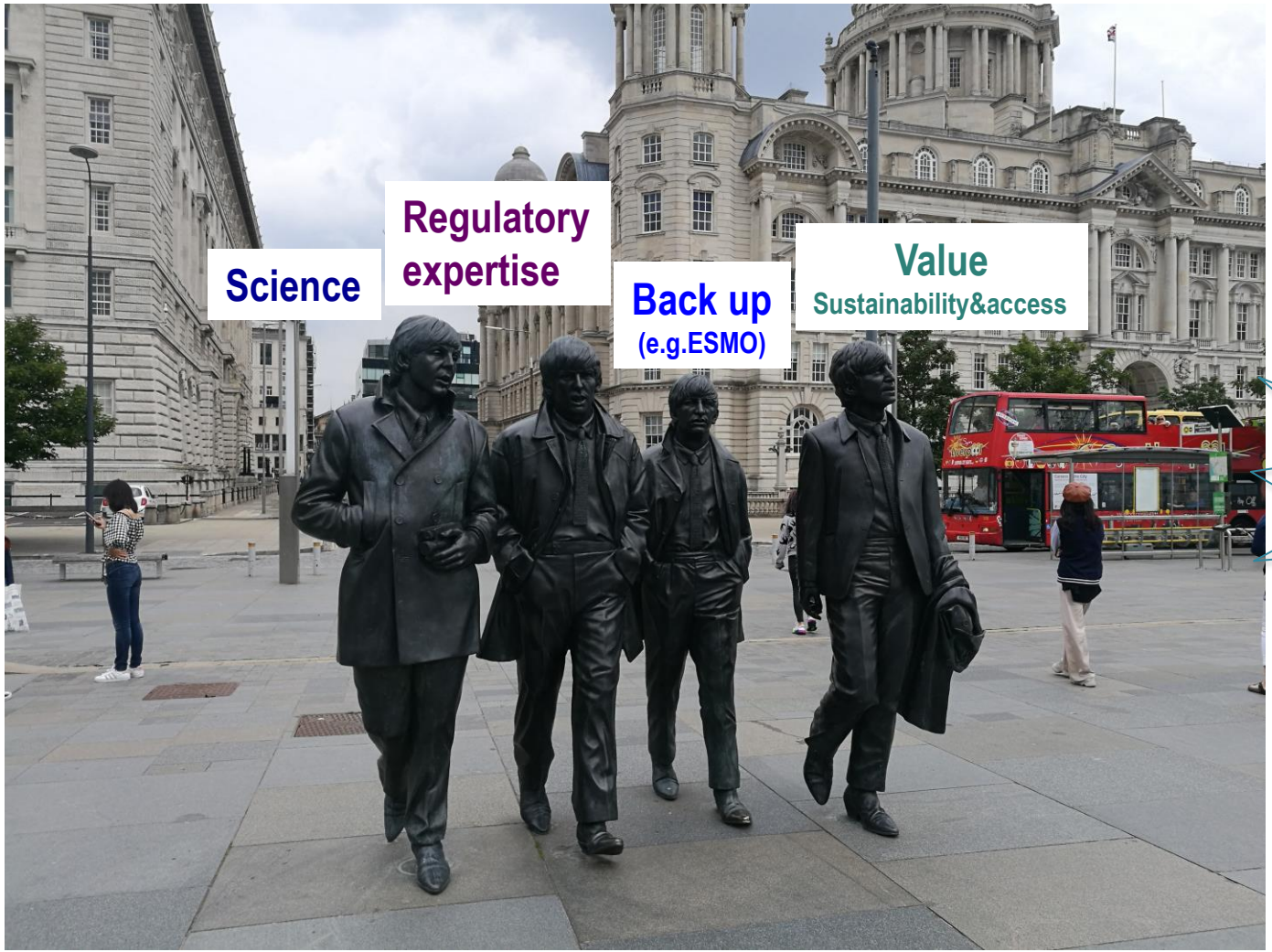
O Compromisso dos Medicamentos Genéricos e Biossimilares

The role of biosimilars in value-based oncology care

Rosa Giuliani

The Clatterbridge Cancer Centre, Liverpool, UK

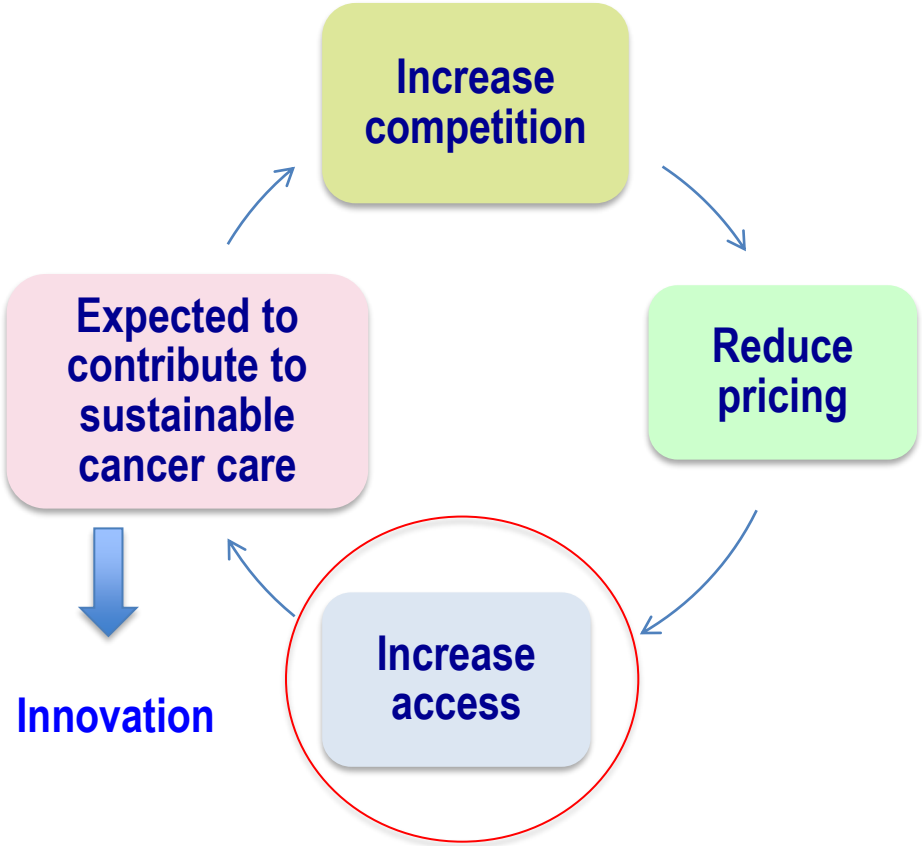
Director of ESMO Public Policy



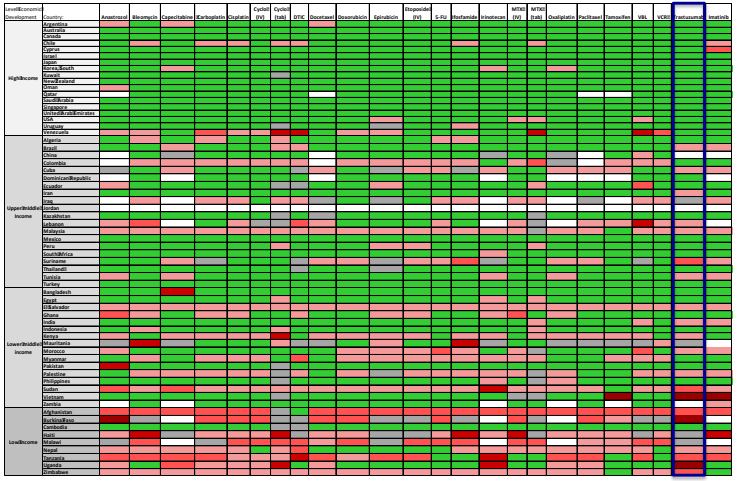
VALUE-based oncology care: the role of biosimilars

Fab Four Pillars

VALUE-based oncology care: the role of biosimilars…is STRAIGHTFORWARD



ESMO CANCER MEDICINES SURVEY INTERNATIONAL: WHO EML AVAILABILITY



Cherny et al, Ann Oncol 2016

ESMO VISION

1 INTEGRATED CANCER CARE
Bridging cancer prevention, research, early-diagnosis, and treatment to improve patient outcomes

2 SPECIALISED EDUCATION
Supporting oncologists in a fast-changing professional environment

3 SUSTAINABLE CANCER CARE
Advocating for equal access to quality treatment and for cancer prevention

2 September 2019

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NHS saves more than £700m on medicines costs

2nd September 2019

The NHS has announced that it has saved more than £700 million from the annual medicines bill to reinvest in new treatments, as part of the Long Term Plan.

The money comes from an NHS-wide campaign, which supported patients and doctors to maximise the use of 'generic' and best value 'biologic' treatments to treat conditions including arthritis and cancer.

NHS England has previously announced plans to accelerate and widen the uptake of best value biologic medicines in a bid to save £400 million to £500 million per year by 2020/21, as the money can then be be reinvested in other "new, innovative and cost-effective treatments".

The new figures show that the uptake of best value medicines lowered costs to taxpayers by £294 million last year alone, on track to meet its ambitious target of a further £400 million annual savings by 2021.

A huge part of that saving was made up by a single drug, AbbVie's Humira (adalimumab), as it came off patent at the end of 2018, allowing for "smart procurement". Previously it was the drug that hospitals spent the most on, as a cost of more than £400m a year.

The NHS also announced that the savings for 2018-19 come on top of the £413 million saved from the annual medicines bill in the previous two years by maximising the use of best value generic and biologic treatments.

Added together, the savings mean the campaign to drive take-up has seen more than £700 million freed up to reinvest in other effective medicines.

Simon Stevens, NHS chief executive, said that the NHS is one of the "most efficient health services in the world", but ensured that "as part of the Long Term Plan, we will continue to drive changes to ensure every NHS pound is spent wisely and patients have access to innovative life changing medicines."

He continued, "Use of the best value versions of expensive medicines is already delivering effective treatment for patients across the NHS, including those with cancer, offering the right care for patients while saving the tax payer hundreds of millions of pounds."

The NHS reminds, however, that the decision to switch to a best value medicine should always be done in consultation with the patient, through shared decision making.

Over £ 700 million from the annual medicines bill to REINVEST in new treatments

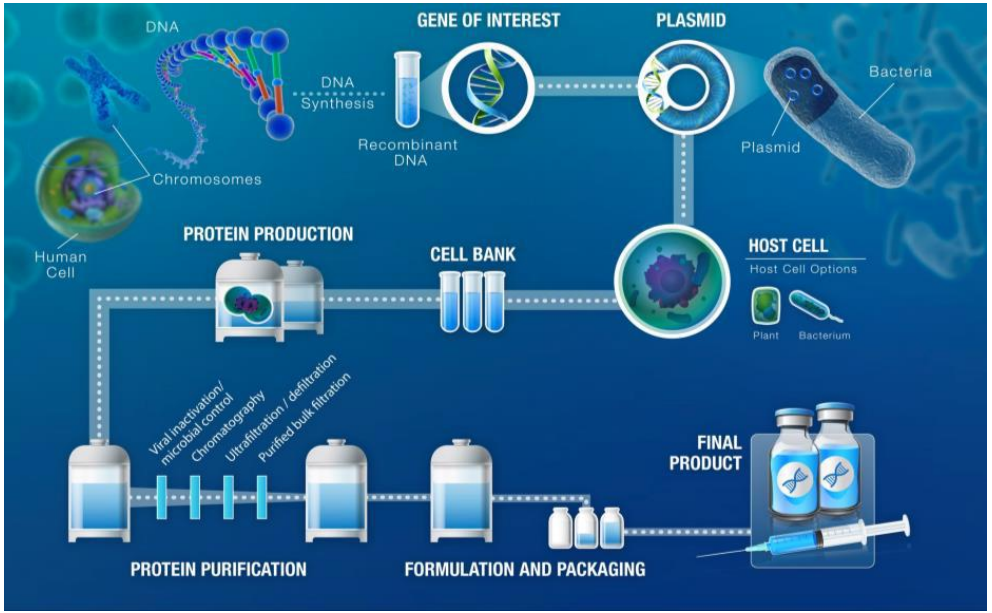
The cumulative savings between 2016 and 2020 in the EU5 and the USA are estimated to range between 49 and 98 billion Euros

Delivering on the Potential of Biosimilar Medicines: The Role of Functioning Competitive Markets Introduction (2016).

http://www.pharmatimes.com/news/nhs_saves_more_than_700m_on_medicines_costs_1300451?utm_source=Virdis+Newsletter&utm_medium=email&utm_campaign=virdis+news+alert

SCIENCE + My EUREKA moments

Changes of originator/reference biologicals are well known



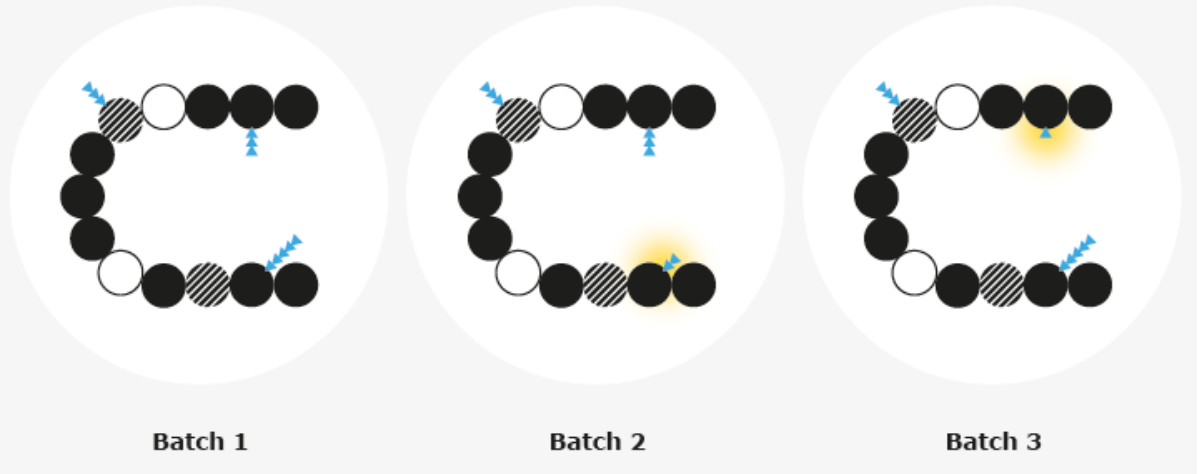
Changes in the manufacturing process after approval include

- -Supplier of cell culture media
- -New purification methods
- -New manufacturing sites

Product changes are closely monitored by regulators

When the **manufacturing process** of the **originator changes** (type II variation) **new data** on safety and efficacy related to the new process **are NOT requested**

Variability between different batches of a biological medicine



Amino acid sequence and biological activity remain the same

EMA/EC Biosimilars in the EU, information guide for HCP

Number of manufacturing changes

Changes of manufacturing must be shown to have

NO impact

on the identity, purity, potency, quality, and safety of product

Vezér et al. Curr Med Res Opin 2016

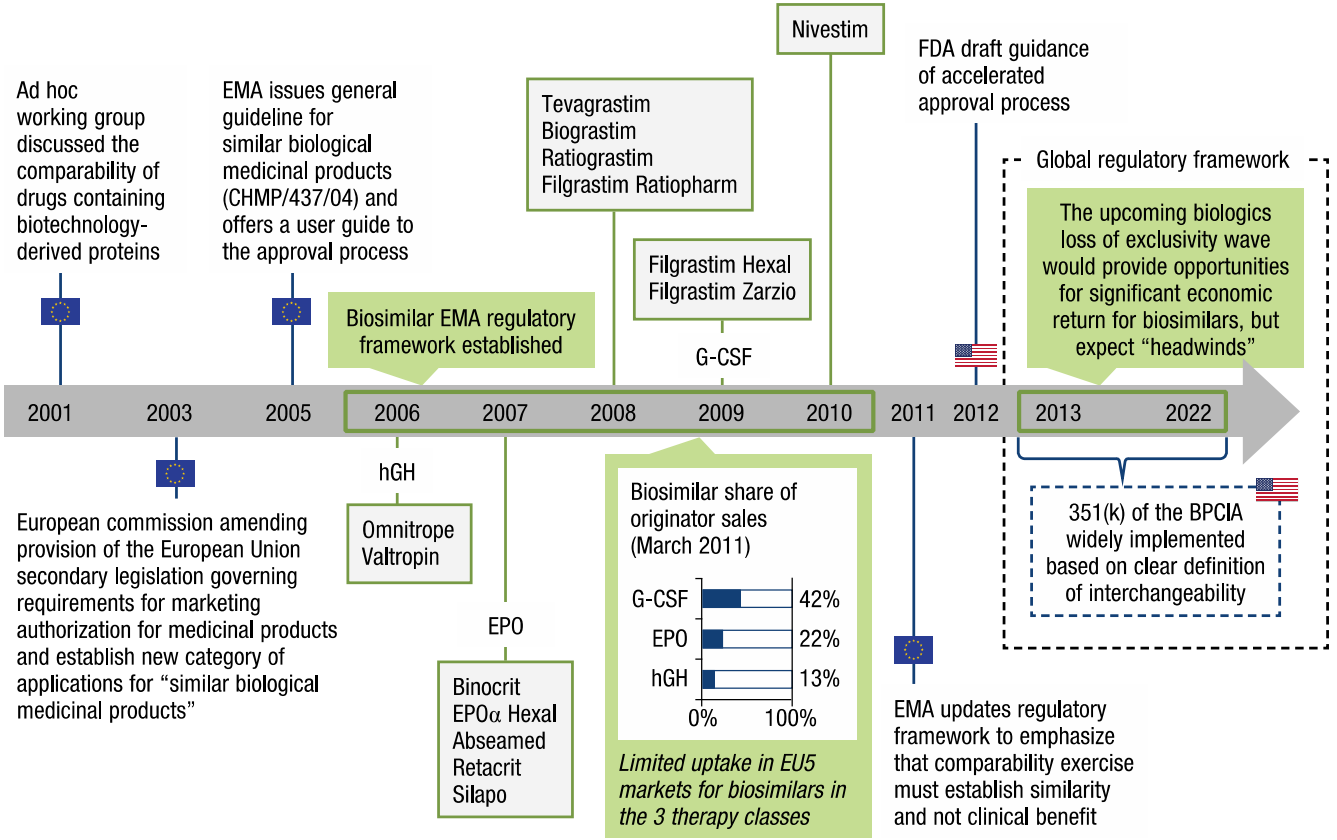
Regulatory development of biosimilars in EU

Rompas Am health and Drug Benefits, 2015

Comparability in a X product following changes in the production process

Comparability of *recombinant drugs* developed by another manufacturer

June 1998 CONCEPT paper On comparability of biotechnology-derived products



Biosimilars in Europe (17 September 2019)*

93 MAAs submitted

80 MAAs reviewed

13 MAAs under review
- Adalimumab (1)
- Bevacizumab (1)
- Etanercept (1)
- Insulin aspart (1)
- Pegfilgrastim (1)
- Rituximab (3)
- Teriparatide (3)
- Trastuzumab (2)

EMA scientific committees and working parties

2 Negative
- Interferon alfa
- Insulin

17 Withdrawn (*pre-approval*)
- Insulin (6)
- Bevacizumab (1)
- Epoetin (1)
- Pegfilgrastim (6)
- Trastuzumab (1)
- Adalimumab (1)
- Infliximab (1)

61 Positive opinions

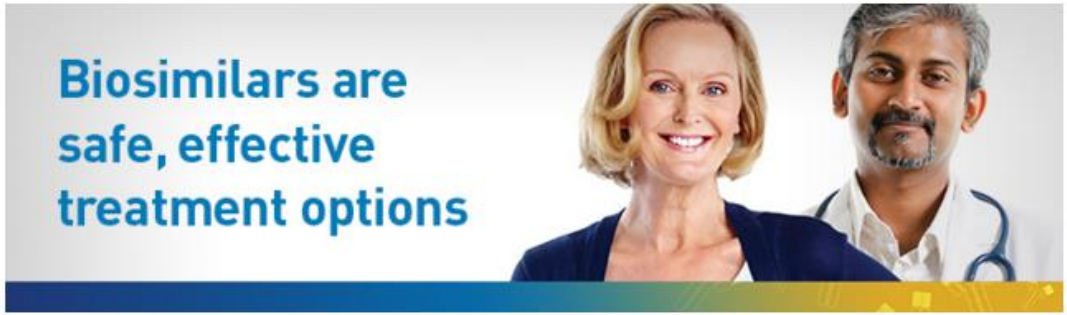
54 MAs
- Somatropin (1)
- Epoetin (5)
- Filgrastim (7)
- Infliximab (4)
- Follitropin alfa (2)
- Etanercept (2)
- Bevacizumab (2)
- Insulin glargine (2)
- Enoxaparin (2)
- Teriparatide (2)
- Rituximab (5)
- Adalimumab (8)
- Insulin lispro (1)
- Trastuzumab (5)
- Pegfilgrastim (6)

0 Awaiting EC decision

7 Withdrawn (*post-approval*)
- Filgrastim (2)
- Somatropin (1)
- Insulin glargine (1)
- Adalimumab (2)
- Rituximab (1)

* Information on the EMA website

Biosimilars



Congress, through the Biologics Price Competition and Innovation Act (BPCI Act) of 2009, created an abbreviated licensure pathway for biological products that are demonstrated to be biosimilar to or interchangeable with an FDA-approved biological product. This pathway was established as a way to provide more treatment options, increase access to lifesaving medications, and

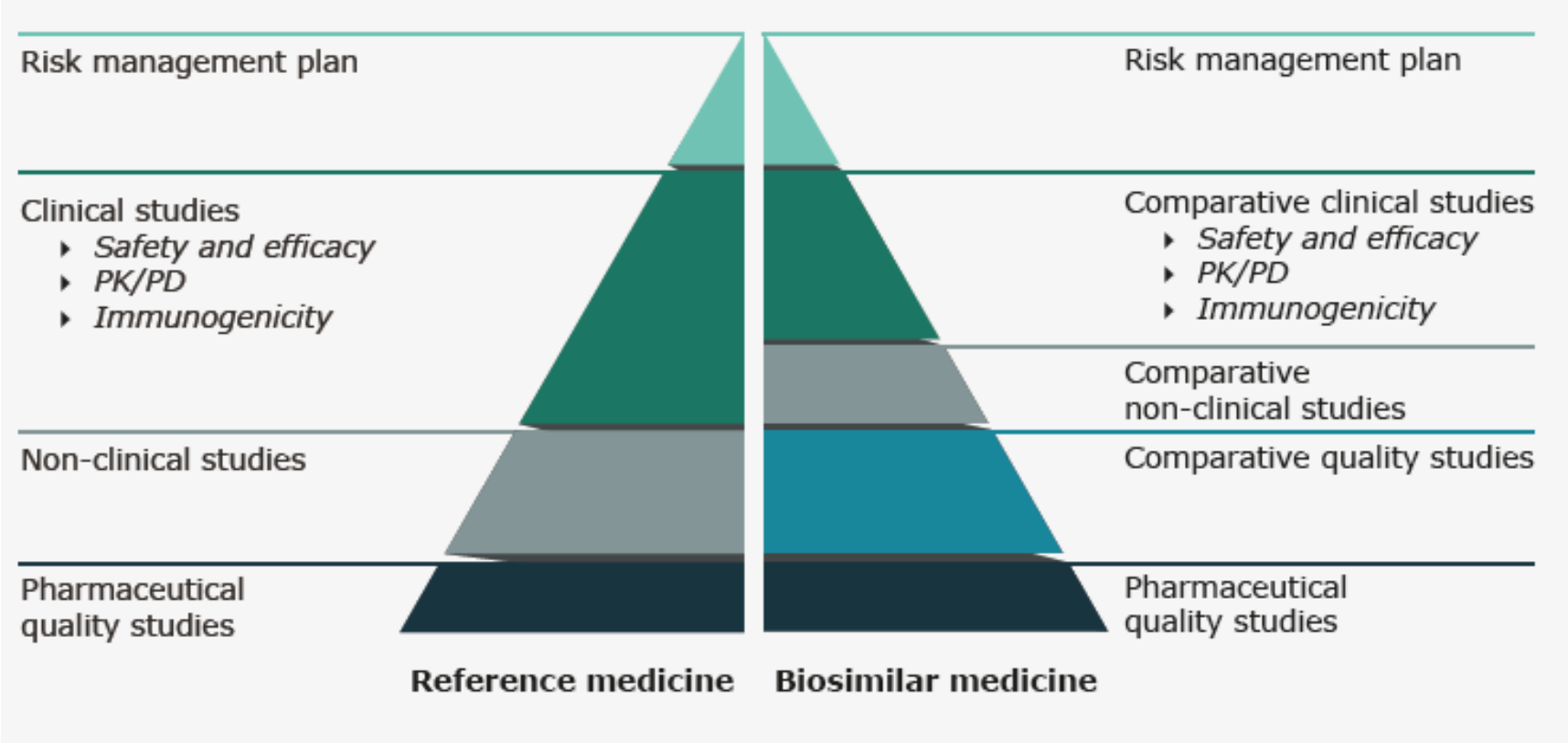
Biosimilars Action Plan (BAP)

New Educational Materials
Learn more about biosimilars and check out our videos, fact sheets, shareable graphics,

https://www.who.int/biologicals/biotherapeutics/similar_biotherapeutic_products/en/

https://www.who.int/medicines/regulation/biotherapeutic_products/en/

Understanding biosimilarity



EMA/EC Biosimilars in the EU, information guide for HCP

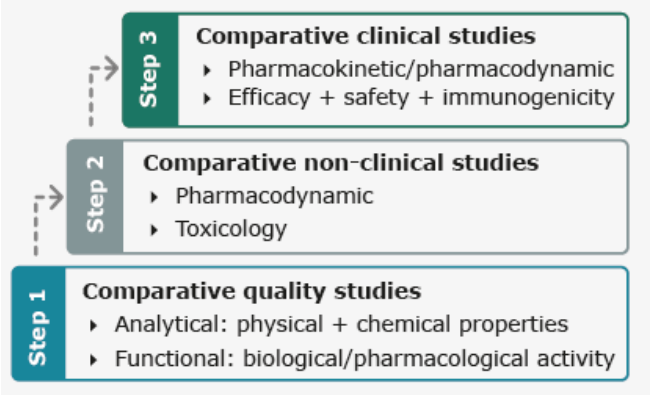
Understanding biosimilarity

Demonstration of clinical effect

Demonstration of similarity

McCamish, Clin Pharmacol Ther, 2012

Step-wise approach for biosimilar development



EMA/EC Biosimilars in the EU, HCP guide

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Human regulatory

Overview | Research and development | Marketing authorisation | Post-authorisation | Herbal products

- Advanced therapies
- Biosimilars
- Compliance
- Data on medicines (ISO IDMP standards)
- Fees
- Orphan designation
- Paediatric medicines
- Pharmacovigilance
- Public health threats
- Support for early access
- Supporting SMEs

Biosimilar medicines

Share

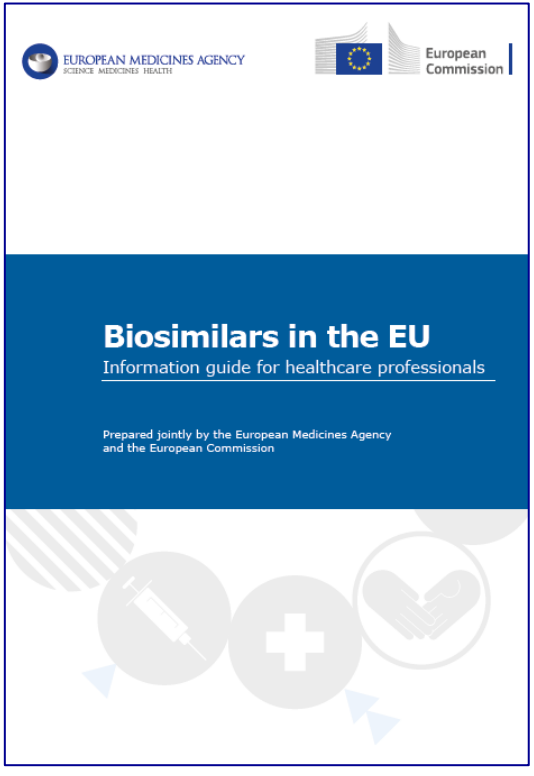
A biosimilar is a biological medicine highly similar to another already approved biological medicine (the 'reference medicine'). Biosimilars are approved according to the same standards of pharmaceutical quality, safety and efficacy that apply to all biological medicines. The European Medicines Agency (EMA) is responsible for evaluating the majority of applications to market biosimilars in the European Union (EU).

Biological medicines offer treatment options for patients with **chronic and often disabling conditions** such as diabetes, autoimmune disease and cancers.

Biological medicines contain active substances from a biological source, such as **living cells or organisms** (human, animals and microorganisms such as bacteria or yeast) and are often produced by cutting-edge technology.

Most biological medicines in current clinical use contain active substances made of **proteins**. These can differ in size and structural complexity, from simple proteins like insulin or growth hormone to more complex ones such as coagulation factors or monoclonal antibodies.

Examples of types of proteins in biological medicines approved in the EU



https://www.ema.europa.eu/en/human-regulatory/overview

Assessment templates and guidance

[insert only for CHMP adopted doc & add EMA header and footer]
London, <insert full date>
<insert Doc. Ref.>
Committee for Medicinal Products for Human Use (CHMP)

<Co>Rapporteur day<60*><80> critical assessment report
Overview and list of questions

Or <DRAFT> CHMP day <90*><120> list of questions
**in case of accelerated assessment*

<Invented name>

<Active Substance>

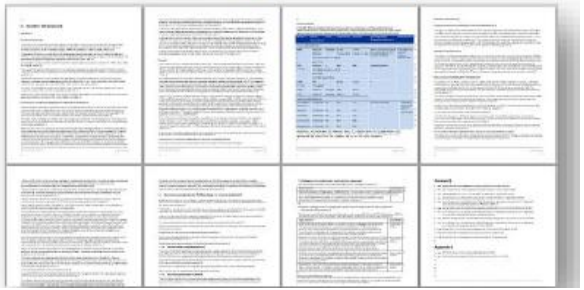
Procedure No. EMEA/H/C/<XXX>

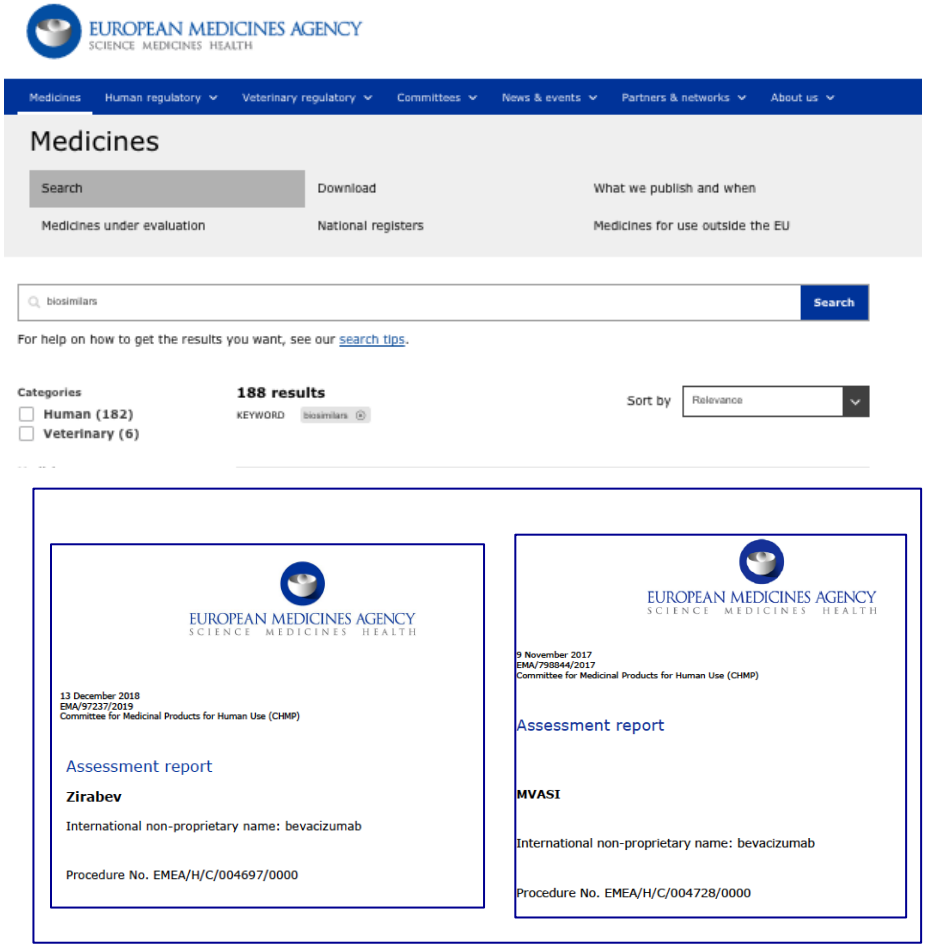
Applicant:

Information for professional audiences

Assessment Report

Expanded the rationale for **extrapolation** and **comparability**

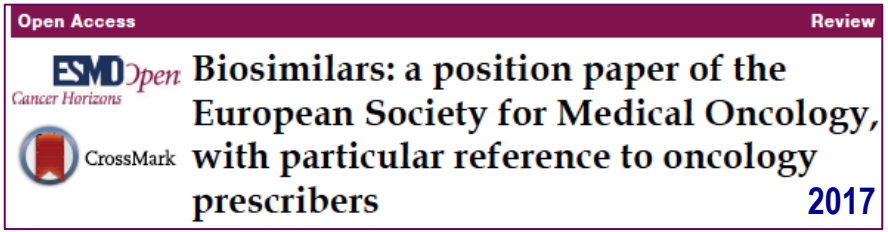




https://www.ema.europa.eu/en/medicines?search_api_views_fulltext=biosimilars

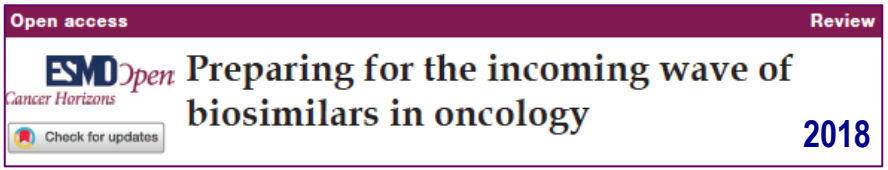
Do I want/ need to discuss clinical trials in detail?
None of them added KEY info to biosimilars development. They confirmed what was already known from analytical studies

The importance of backing up science: ESMO position



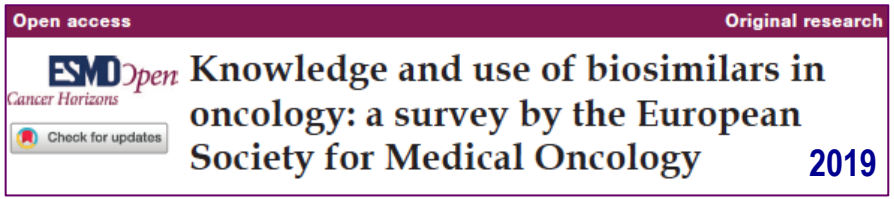
Position paper

CLEAR VISION



ESMO Special session during ESMO 2017 in Madrid (700 participants)
"The incoming wave of biosimilars In oncology"

FOSTERING Dialogue and knowledge



ESMO survey on awareness on Biosimilars launched during ESMO2017 in Madrid. Presented @ ESMO colloquium (ESMO 2018, Munich)

ADDRESSING gaps In education to remove barriers

ESMO

GOOD SCIENCE
BETTER MEDICINE
BEST PRACTICE

Welcome to the **EUROPEAN SOCIETY FOR MEDICAL ONCOLOGY**, the leading European professional organisation for medical oncology.

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ESMO / POLICY / ESMO Biosimilars Portal

» ESMO Biosimilars Portal

- Science
- Education
- Regulation
- Patient Resources

ESMO Biosimilars Portal

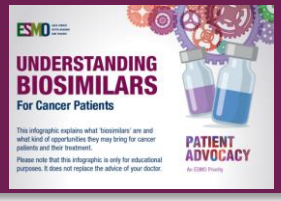
https://www.esmo.org/Policy/ESMO-Biosimilars-Portal

BIOSIMILARS

Ongoing projects

Education

- 2 E-learning modules for oncologists and patients
- Infographic for patients (to be translated in different languages)



Awareness

- Tool: Dedicated biosimilars page & portal on ESMO website
- Survey with nurses – ongo

Engagement

Representing clinician's perspective in various meetings (Medicines for Europe, regulatory agencies, DIA etc)

Regular sessions at ESMO Congresses

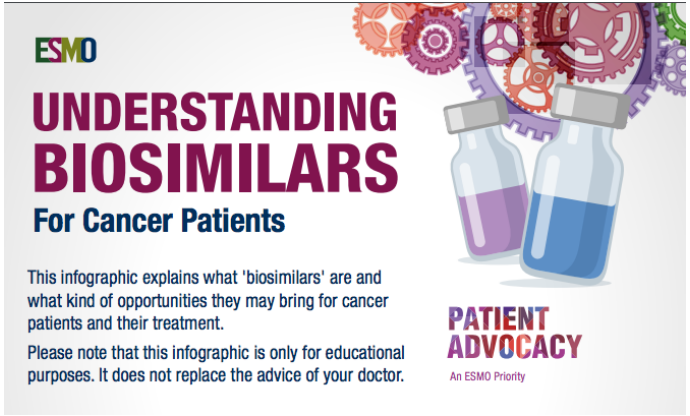
Papers

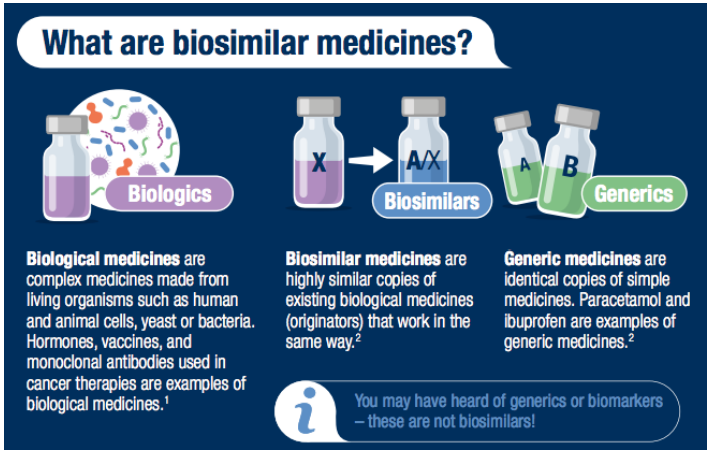
ESMO survey results paper Knowledge and use of biosimilars in oncology: a survey by the European Society for Medical Oncology (2019)

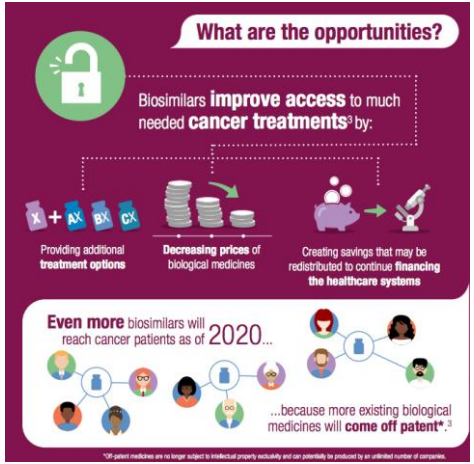
Preparing for the incoming wave of biosimilars in oncology (2018)

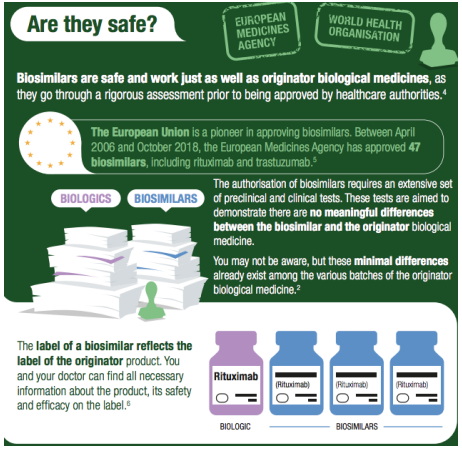
ESMO Position paper on biosimilars (2016)

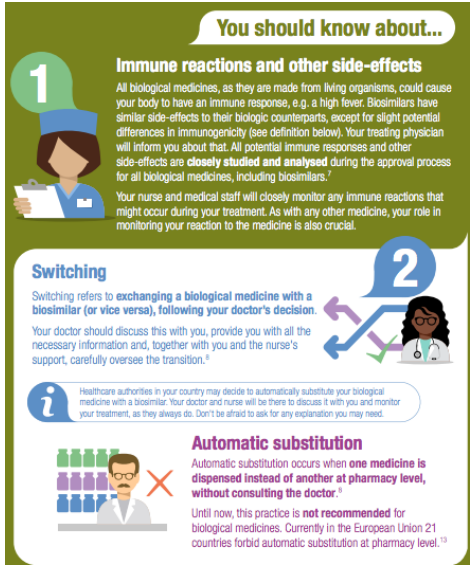
EDUCATION: patients' infographic

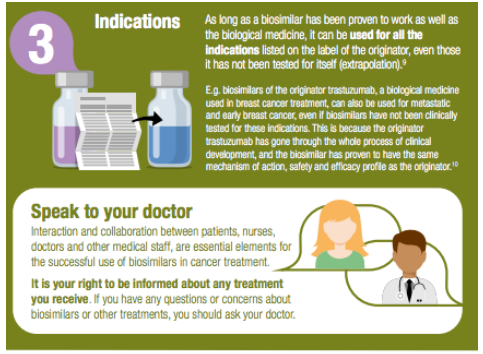


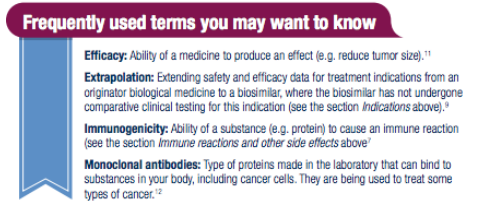












Journal Pre-proof

Sept 2020

5th ESO-ESMO international consensus guidelines for advanced breast cancer (ABC 5)†

F. Cardoso, S. Paluch-Shimon, E. Senkus, G. Curigliano, M.S. Aapro, F. André, C.H. Barrios, J. Bergh, G.S. Bhattacharyya, L. Biganzoli, F. Boyle, M.-J. Cardoso, L.A. Carey, J. Cortés, N.S. El Saghir, M. Elzayat, A. Eniu, L. Fallowfield, P.A. Francis, K. Gelmon, J. Gligorov, R. Haidinger, N. Harbeck, X. Hu, B. Kaufman, R. Kaur, B.E. Kiely, S.-B. Kim, N.U. Lin, S.A. Mertz, S. Neciosup, B.V. Offersen, S. Ohno, O. Pagani, A. Prat, F. Penault-Llorca, H.S. Rugo, G.W. Sledge, C. Thomssen, D.A. Vorobiof, T. Wiseman, B. Xu, L. Norton, A. Costa, E.P. Winer

CONSENSUS GUIDELINES

General statements: affordability/cost effectiveness		
The medical community is aware of the problems raised by the cost of ABC treatment. Balanced decisions should be made in all instances; patients' well-being, length of life and preferences should always guide decisions.	Expert opinion/A	100%
We strongly recommend the use of objective scales, such as the **ESMO-MCBS** or the **ASCO Value Framework**, to evaluate the real magnitude of benefit provided by a new treatment and help prioritise funding, particularly in countries with limited resources.	Expert opinion/A	88%
The ABC community strongly supports the use of **biosimilars** both for treatment of breast cancer (i.e. trastuzumab) and for supportive care (i.e. growth factors). To be used, the biosimilar must be approved after passing the stringent development and validation processes required by the EMA or the FDA or other similarly strict authority.	I/A	90%

WHY are we still discussing the role of biosimilars?

It is not a rethorical question

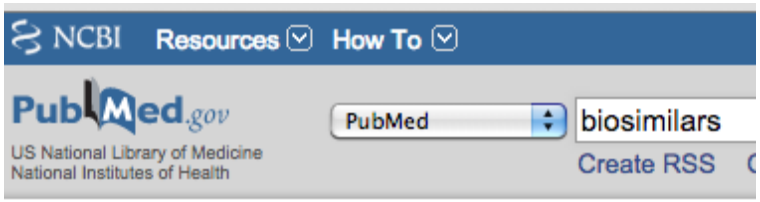
Are clinical efficacy trial needed?

Regulatory experience and technological advances (high performing analytical tools)

Never added crucial information about biosimilars

Do we need EXTRA-monitoring? NO

Pharmacovigilance systems and Risk Management plan are robust



-Biosimilars: do they exist?

-Biosimilars: how similars are there?

2004

2008

-Barriers to the use..

-The challenge of…

-Paving the way for…

2018/9

-The rise of biosimilars

-Are biosimilars the future in oncology/haematology?

The End of Phase 3 Clinical Trials in Biosimilars development?

Requirements for an application without an efficacy trial

Prerequisites for the reference product

Biosimilar development starts with in-depth knowledge of the RP. Its main and potential secondary MOAs in the target diseases need to be known and demonstrable. As a result, the physicochemical and functional properties that are more likely to relate to the clinical outcomes will be identified, which will allow definition of critical quality attributes (CQA); that is, the quality attributes that would need to be controlled or maintained within appropriate limits or ranges to ensure that clinical effects of the product are not impacted. If the main MOA of a complex RP is unknown, it is likely that an efficacy trial will be required.

The PK, efficacy, safety, and immunogenicity profiles of the RP need to be well characterised and the impact of ADAs on PK (increased or decreased clearance), efficacy (neutralising ADAs), and safety (injection-related reactions) need to be known. Population PK or PK–PD models available in the literature should be taken into consideration [28]. If there are notable uncertainties around these clinical aspects, the need for a comparative efficacy/safety trial is likely.

DRUDIS-2770; No of Pages 9 ARTICLE IN PRESS

Drug Discovery Today • Volume 00, Number 00 • September 2020 PERSPECTIVE

ELSEVIER

Streamlined approval of biosimilars: moving on from the confirmatory efficacy trial

Marie-Christine Bielsky, marie.bielsky@mhra.gov.uk, Anne Cook, Andrea Wallington, Andrew Exley, Shahin Kauser, Justin L. Hay, Leonard Both and David Brown

Knowledge of RP

- **MoA**
- **Clinical Quality Attribute**
- **PK, efficacy, safety, immunogenicity**

YES → **No clinical trial needed**

NO → **Clinical trial needed**

HOW TO BUILD → HOW TO CONSOLIDATE CONFIDENCE

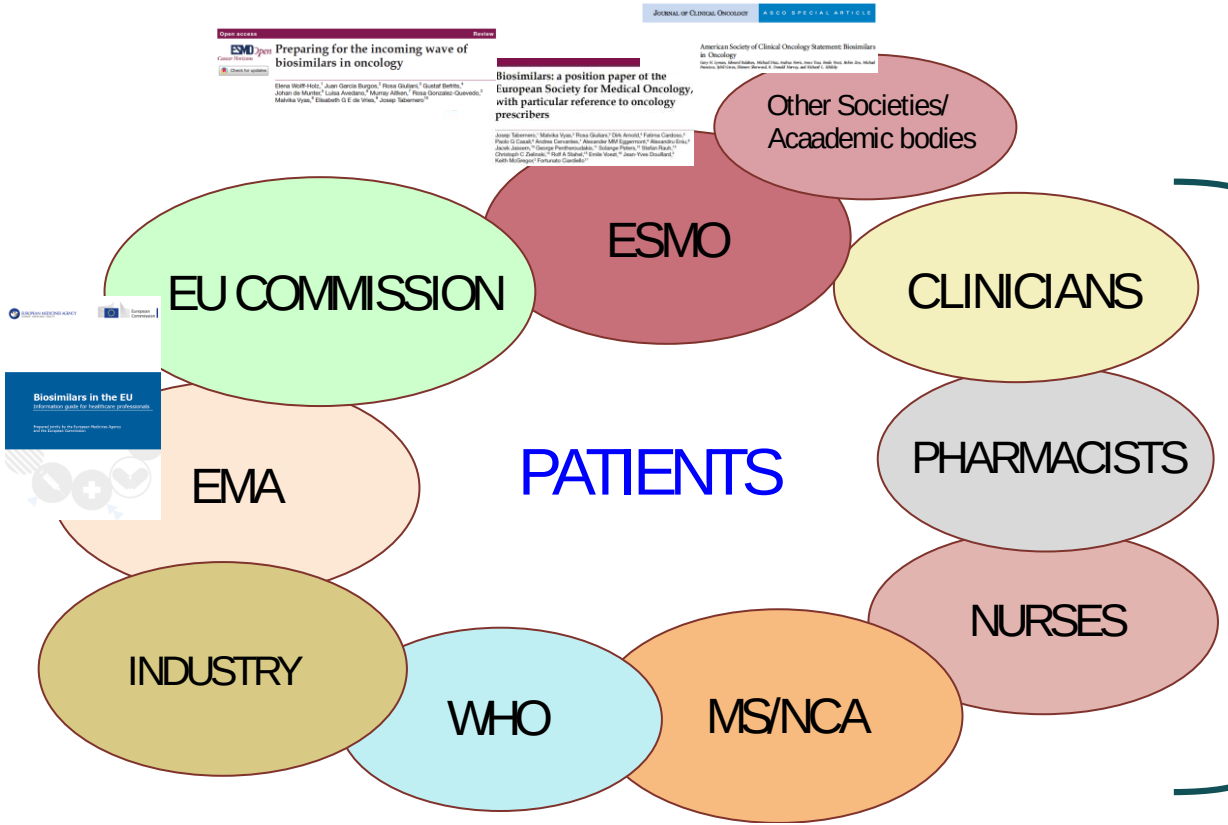
SCIENCE

GUIDANCE

INTERACTION/ COLLABORATION

DATA COLLECTION

DATA ANALYSIS



End users + data generators

Capture Data Systems (registries, PhVig, et cet…)

SUCCESSFUL IMPLEMENTATION

SCIENCE

Confidence

SCIENCE

REGULATORY EXPERTISE