

E-Conference

Valor em Saúde

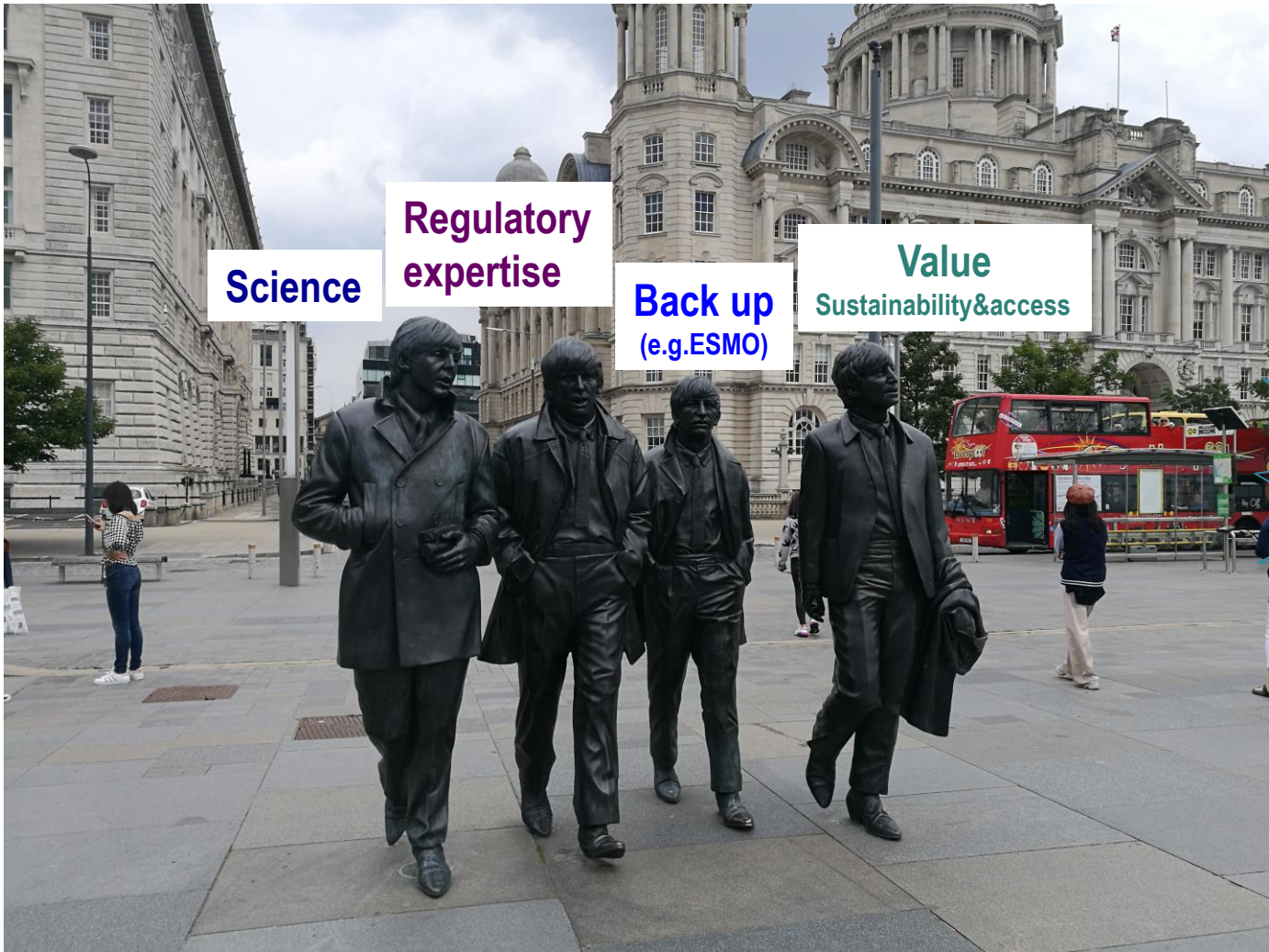
O Compromisso dos Medicamentos
Genéricos e Biossimilares

The role of biosimilars in value-based oncology care

Rosa Giuliani

The Clatterbridge Cancer Centre, Liverpool, UK

Director of ESMO Public Policy



Science

**Regulatory
expertise**

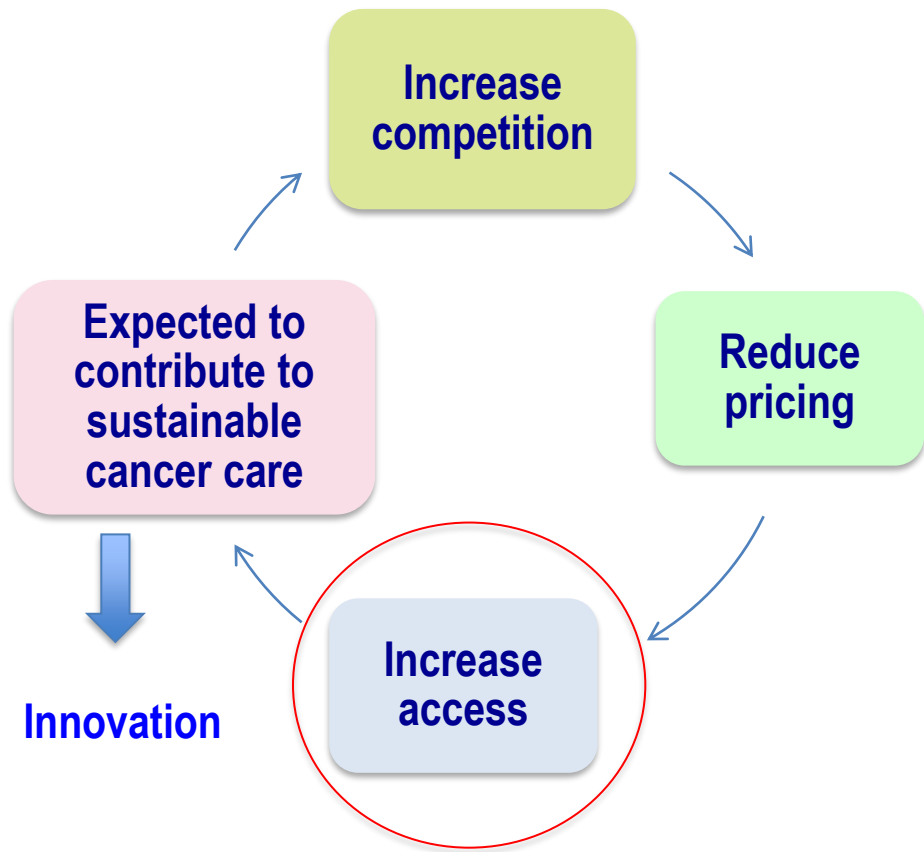
Back up
(e.g. ESMO)

Value
Sustainability & access

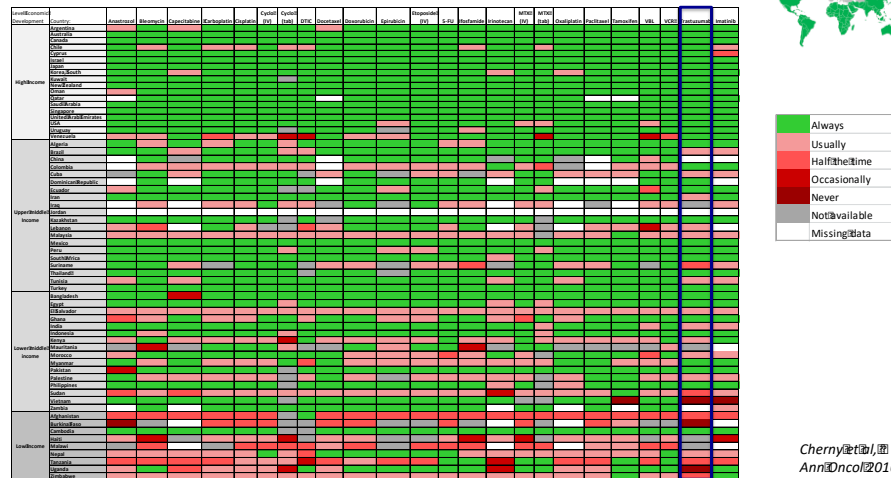
**VALUE-based
oncology care:
the role of
biosimilars**

**Fab Four
Pillars**

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



ESMO CANCER MEDICINES SURVEY INTERNATIONAL: WHO EML AVAILABILITY



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

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 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.

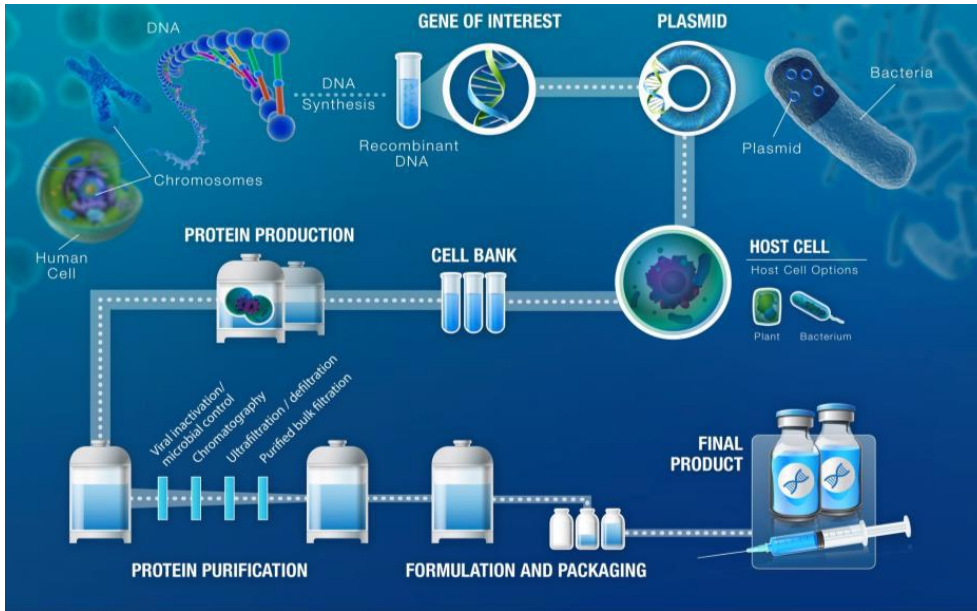
**Over £ 700 million from the
annual medicines bill
to REINVEST
in new treatments**

**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).*

SCIENCE + My EUREKA moments

Changes of originator/reference biologicals are well known



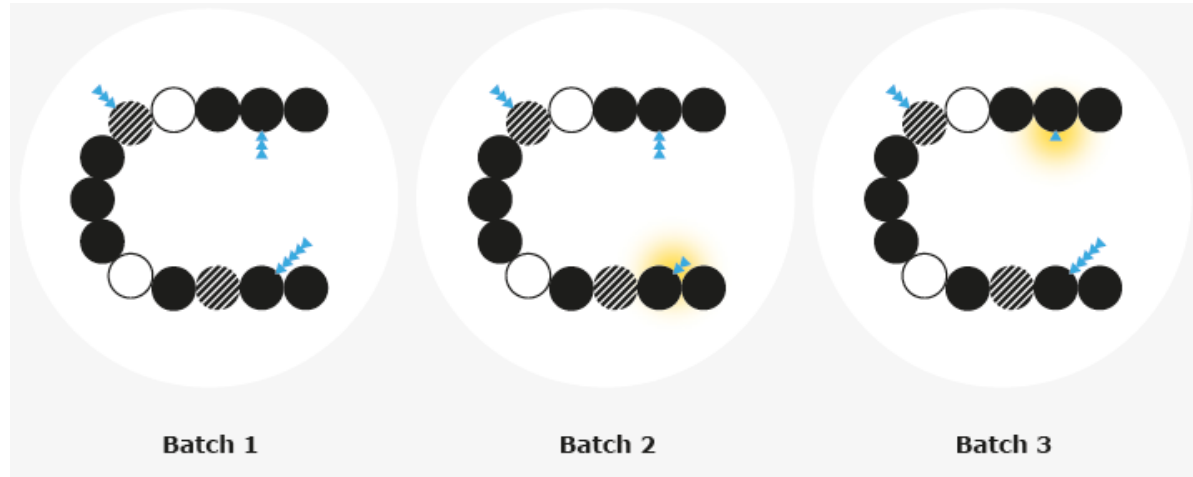
Changes in the manufacturing process after approval include

- 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**

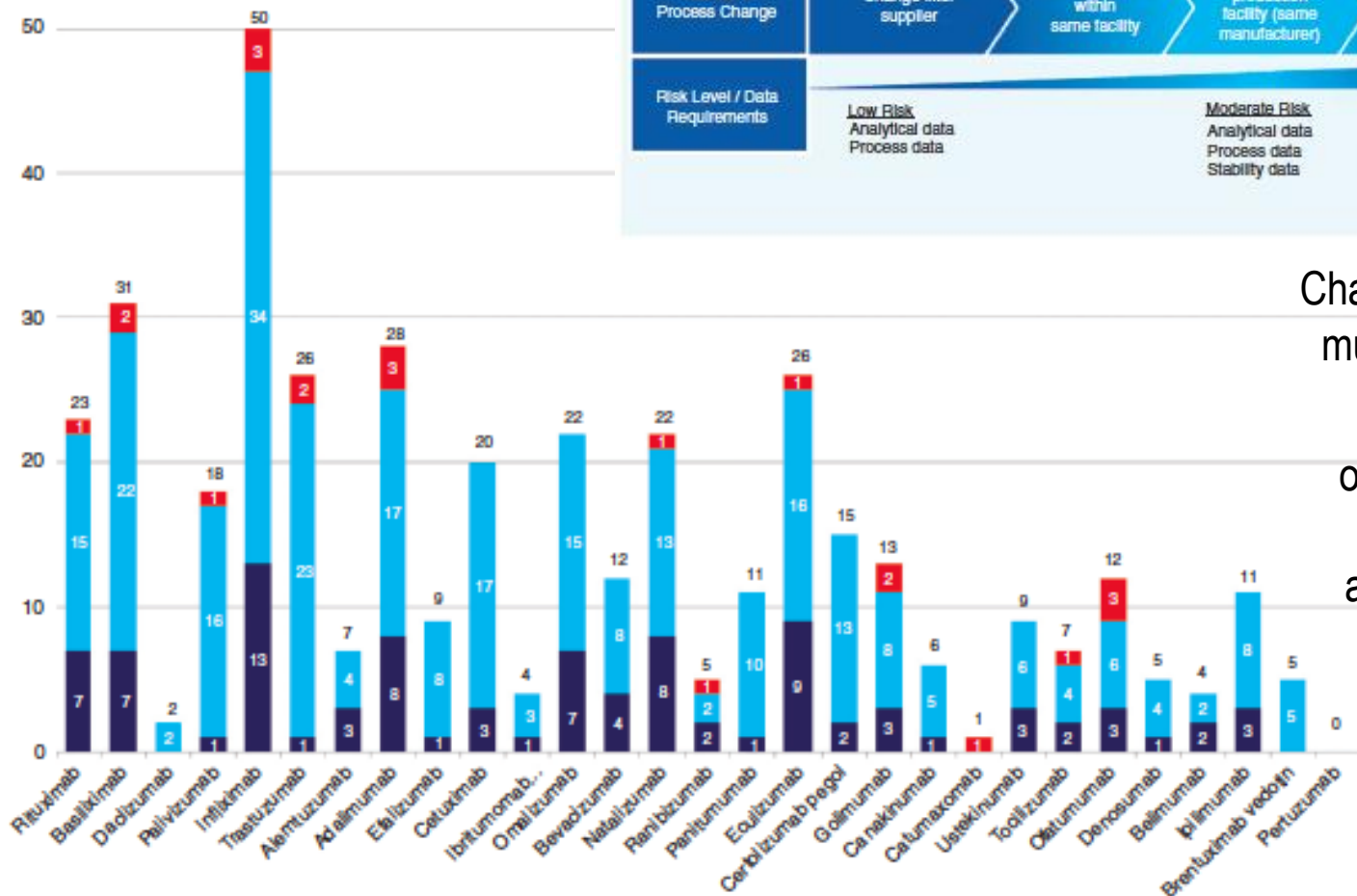
Variability between different batches of a biological medicine



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

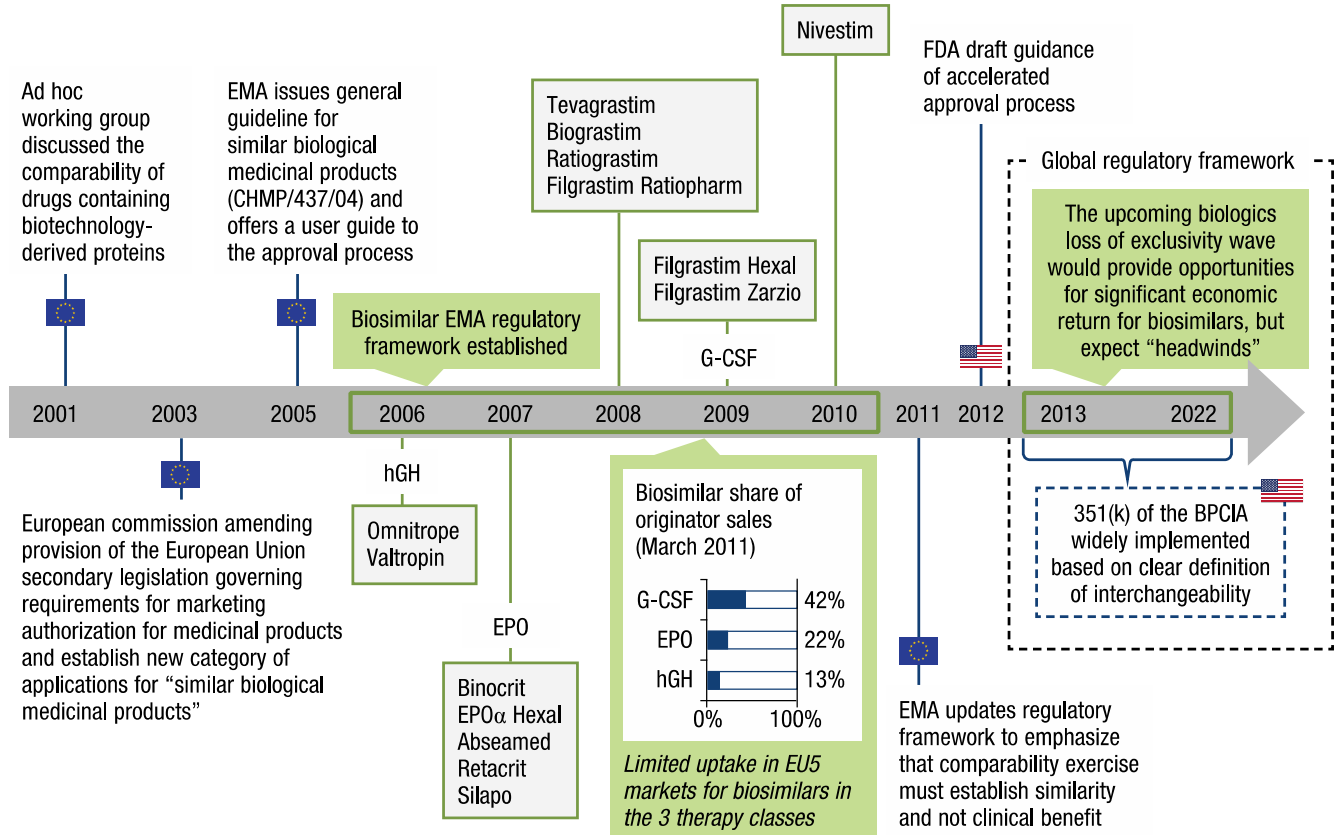
Regulatory development of biosimilars in EU

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)*



EUROPEAN MEDICINES AGENCY

80

MAAs reviewed

93

MAAs submitted

13

MAAs under review

Adalimumab (1)
Bevacizumab (1)
Etanercept (1)
Insulin aspart (1)
Pegfilgrastim (1)
Rituximab (3)
Teriparatide (3)
Trastuzumab (2)

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

MAAs

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)



EMA scientific
committees and
working parties

0

Awaiting EC decision

7

Withdrawn (*post-approval*)

Filgrastim (2)
Somatropin (1)
Insulin glargine (1)
Adalimumab (2)
Rituximab (1)



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Drugs

[Home](#) > [Drugs](#) > [Development & Approval Process \(Drugs\)](#) > [How Drugs are Developed and Approved](#) > [Types of Applications](#) > [Therapeutic Biologic Applications \(BLA\)](#) > [Biosimilars](#)

Biosimilars

[Biosimilar and Interchangeable Products](#)

[Biosimilar Development, Review, and Approval](#)

[Prescribing Biosimilar and Interchangeable Products](#)

[Biosimilar Product Information](#)

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Biosimilars



SHARE



TWEET



LINKEDIN



PIN IT



EMAIL



PRINT

**Biosimilars are
safe, effective
treatment options**



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

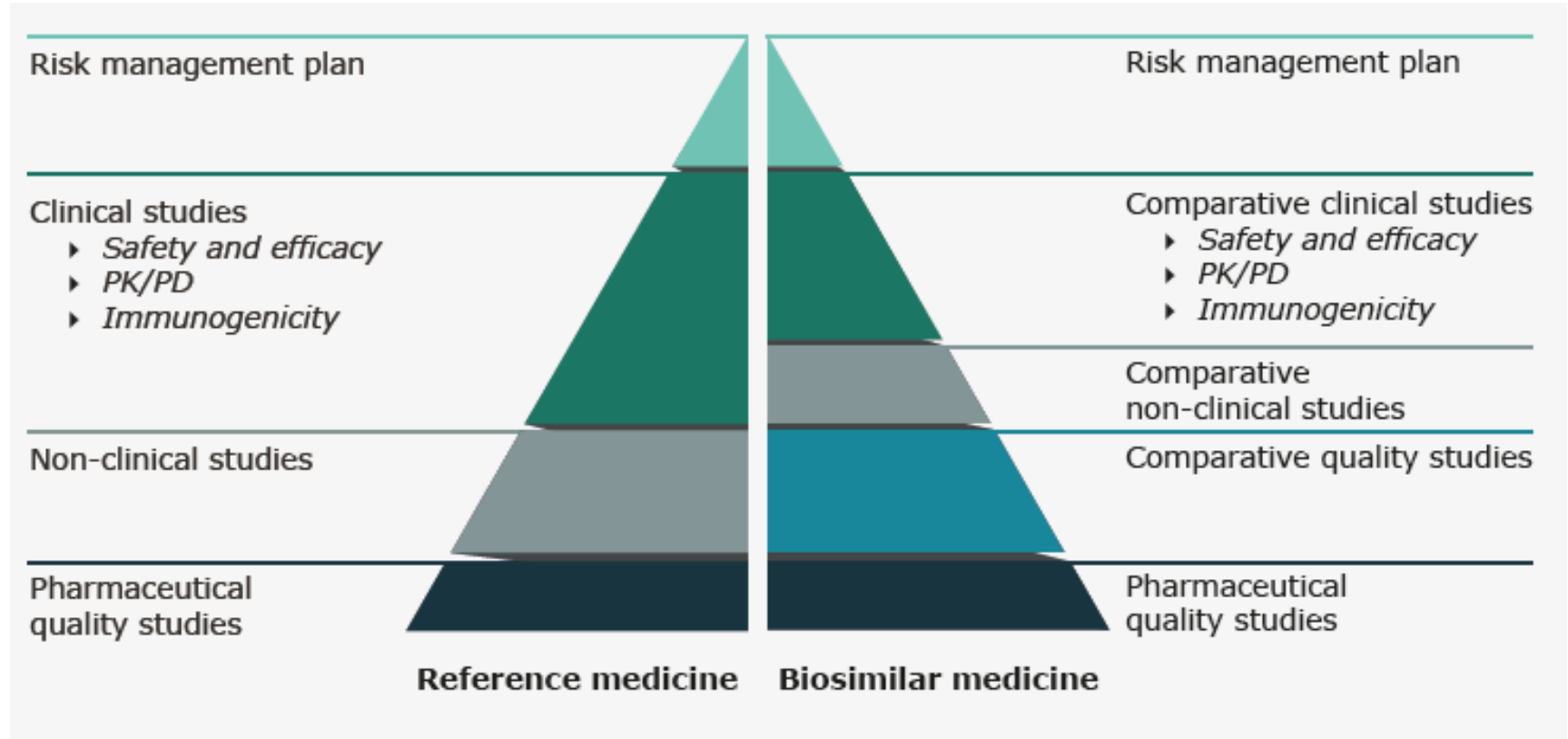
[Learn more about biosimilars and check out our videos, fact sheets, shareable graphics,](#)



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

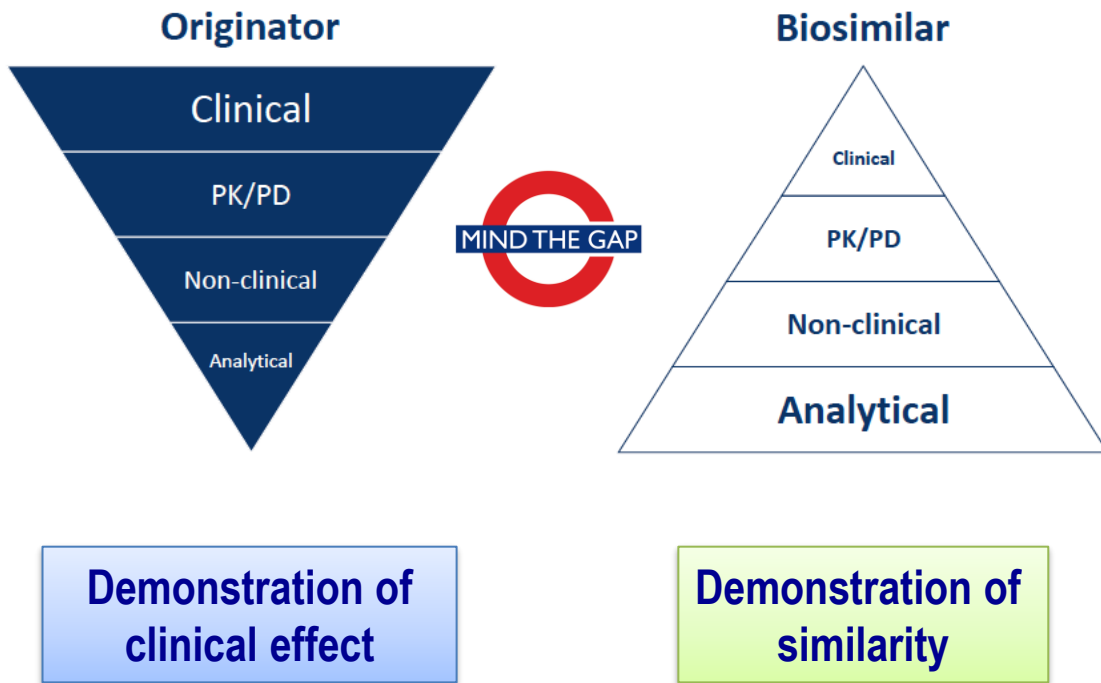
https://www.who.int/medicines/regulation/biotherapeutic_products/en/

Understanding biosimilarity



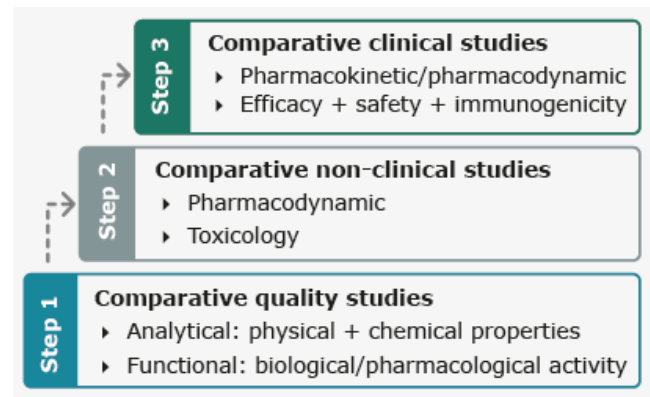
EMA/EC Biosimilars in the EU, information guide for HCP

Understanding biosimilarity



McCamish, Clin Pharmacol Ther, 2012

Step-wise approach for biosimilar development



*EMA/EC Biosimilars
in the EU, HCP guide*

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

Biosimilars in the EU

Information guide for healthcare professionals

Prepared jointly by the European Medicines Agency
and the European Commission



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**



6. <Biosimilarity assessment>	82
6.1. Comparability exercise and indications claimed	82
6.2. Results supporting biosimilarity	82
6.3. Uncertainties and limitations about biosimilarity	82
6.4. Discussion on biosimilarity	82
6.5. Extrapolation of safety and efficacy	83
6.6. Additional considerations	83
6.7. Conclusions on biosimilarity and benefit risk balance	83



Medicines

Search

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Medicines under evaluation

National registers

Medicines for use outside the EU

biosimilars

Search

For help on how to get the results you want, see our [search tips](#).

Categories

- ☐ Human (182)
☐ Veterinary (6)

188 results

KEYWORD biosimilars

Sort by

Relevance



EUROPEAN MEDICINES AGENCY
SCIENCE · MEDICINES · HEALTH

13 December 2018
EMA/97237/2019
Committee for Medicinal Products for Human Use (CHMP)

Assessment report

Zirabev

International non-proprietary name: bevacizumab

Procedure No. EMEA/H/C/004697/0000



EUROPEAN MEDICINES AGENCY
SCIENCE · MEDICINES · HEALTH

9 November 2017
EMA/790344/2017
Committee for Medicinal Products for Human Use (CHMP)

Assessment report

MVASI

International non-proprietary name: bevacizumab

Procedure No. EMEA/H/C/004728/0000



EUROPEAN MEDICINES AGENCY
SCIENCE · MEDICINES · HEALTH

14 December 2017
EMA/44005/2018
Committee for Medicinal Products for Human Use (CHMP)

Assessment report

Herzuma

International non-proprietary name: trastuzumab

Procedure No. EMEA/H/C/002575/0000



EUROPEAN MEDICINES AGENCY
SCIENCE · MEDICINES · HEALTH

22 March 2018
EMA/CHMP/261937/2018
Committee for Medicinal Products for Human Use (CHMP)

Assessment report

KANJINTI

International non-proprietary name: trastuzumab

Procedure No. EMEA/H/C/004361/0000



EUROPEAN MEDICINES AGENCY
SCIENCE · MEDICINES · HEALTH

14 September 2017
EMA/CHMP/9835/2018
Committee for Medicinal Products for Human Use (CHMP)

Assessment report

Ontruzant

International non-proprietary name: trastuzumab

Procedure No. EMEA/H/C/004323/0000



EUROPEAN MEDICINES AGENCY
SCIENCE · MEDICINES · HEALTH

31 May 2018
EMA/414092/2018
Committee for Medicinal Products for Human Use (CHMP)

Assessment report

Trazimera

International non-proprietary name: trastuzumab

Procedure No. EMEA/H/C/004463/0000



EUROPEAN MEDICINES AGENCY
SCIENCE · MEDICINES · HEALTH

18 October 2018
EMA/810499/2018
Committee for Medicinal Products for Human Use (CHMP)

Assessment report

Ogivri

International non-proprietary name: trastuzumab

Procedure No. EMEA/H/C/004916/0000

Do I want/ need to discuss clinical trials in detail?

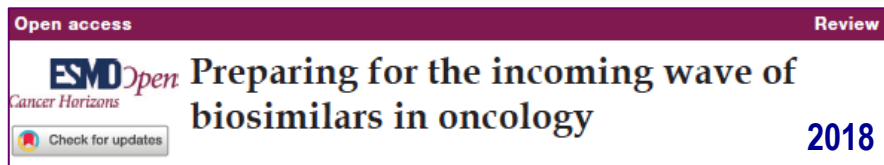
None of them added KEY info to biosimilars development. They confirmed what was already known from analytical studies

The importance of backing up science: ESMO position



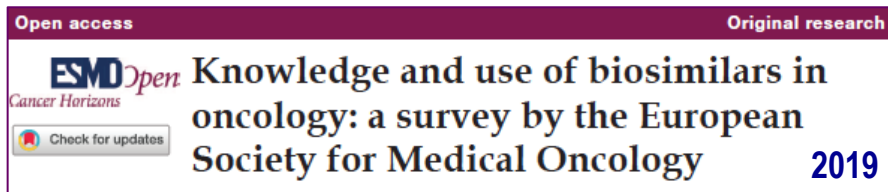
Position paper

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



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 Biosimilars Portal



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[Patient Resources](#)



**Biosimilars promote access
to innovative cancer medicines**

Elisabeth de Vries
Chair of ESMO Cancer
Medicines Committee

**and the sustainability
of health systems**

Josep Tabernero
ESMO President



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

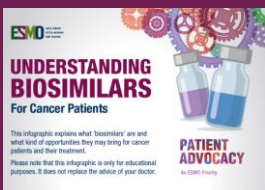
BIOSIMILARS

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** – ongoing



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

ESMO

UNDERSTANDING BIOSIMILARS For Cancer Patients

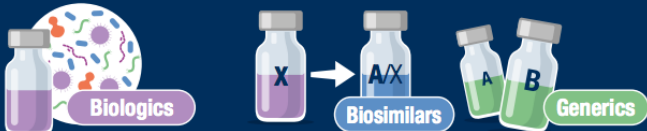
This infographic explains what 'biosimilars' are and what kind of opportunities they may bring for cancer patients and their treatment.

Please note that this infographic is only for educational purposes. It does not replace the advice of your doctor.

PATIENT ADVOCACY
An ESMO Priority



What are biosimilar medicines?



Biologics

Biosimilars

Generics

Biological medicines are complex medicines made from living organisms such as human and animal cells, yeast or bacteria. Hormones, vaccines, and monoclonal antibodies used in cancer therapies are examples of biological medicines.¹

Biosimilar medicines are highly similar copies of existing biological medicines (originators) that work in the same way.²

Generic medicines are identical copies of simple medicines. Paracetamol and ibuprofen are examples of generic medicines.²

i You may have heard of generics or biomarkers – these are not biosimilars!

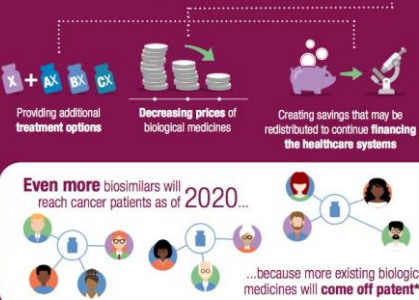
What are the opportunities?

Biosimilars **improve access** to much needed **cancer treatments**³ by:

- Providing additional treatment options
- Decreasing prices of biological medicines
- Creating savings that may be redistributed to continue financing the healthcare systems

Even more biosimilars will reach cancer patients as of 2020...
...because more existing biological medicines will **come off patent**.³

*Off patent medicines are no longer subject to intellectual property exclusivity and can potentially be produced by an unlimited number of companies.



You should know about...

1 Immune reactions and other side-effects

All biological medicines, as they are made from living organisms, could cause your body to have an immune response, e.g. a high fever. Biosimilars have similar side-effects to their biologic counterparts, except for slight potential differences in immunogenicity (see definition below). Your treating physician will inform you about that. All potential immune responses and other side-effects are **closely studied and analysed** during the approval process for all biological medicines, including biosimilars.⁷

Your nurse and medical staff will closely monitor any immune reactions that might occur during your treatment. As with any other medicine, your role in monitoring your reaction to the medicine is also crucial.

Switching

Switching refers to exchanging a biological medicine with a biosimilar (or vice versa), following your doctor's decision.

Your doctor should discuss this with you, provide you with all the necessary information and, together with you and the nurse's support, carefully oversee the transition.⁸

2

Automatic substitution

Automatic substitution occurs when **one medicine is dispensed instead of another at pharmacy level, without consulting the doctor**.⁹

Until now, this practice is **not recommended** for biological medicines. Currently in the European Union 21 countries forbid automatic substitution at pharmacy level.¹⁰

i Healthcare authorities in your country may decide to automatically substitute your biological medicine with a biosimilar. Your doctor and nurse will be there to discuss it with you and monitor your treatment, as they always do. Don't be afraid to ask for any explanation you may need.



Are they safe?

Biosimilars are safe and work just as well as originator biological medicines, as they go through a rigorous assessment prior to being approved by healthcare authorities.⁴

The European Union is a pioneer in approving biosimilars. Between April 2006 and October 2018, the European Medicines Agency has approved **47** biosimilars, including rituximab and trastuzumab.⁵

The authorisation of biosimilars requires an extensive set of preclinical and clinical tests. These tests are aimed to demonstrate there are **no meaningful differences between the biosimilar and the originator biological medicine**.

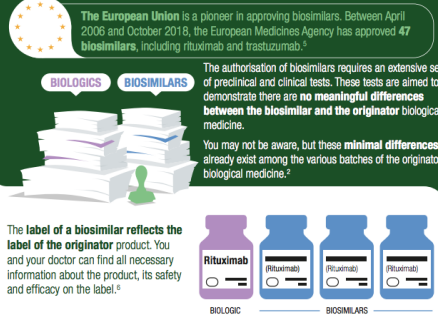
You may not be aware, but these **minimal differences** already exist among the various batches of the originator biological medicine.⁶

BIOTICS BIOSIMILARS

The label of a biosimilar reflects the label of the originator product. You and your doctor can find all necessary information about the product, its safety and efficacy on the label.⁶

Rituximab **trastuzumab** **rituximab** **trastuzumab**

BIOLOGIC BIOSIMILARS



3 Indications

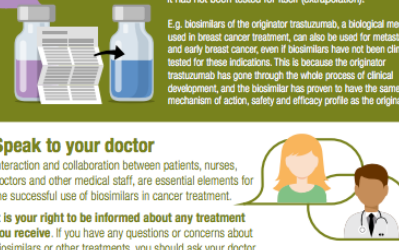
As long as a biosimilar has been proven to work as well as the biological medicine, it can be used for **all the indications** listed on the label of the originator, even those it has not been tested for itself (extrapolation).⁹

E.g. biosimilars of the originator trastuzumab, a biological medicine used in breast cancer treatment, can also be used for metastatic and early breast cancer, even if biosimilars have not been clinically tested for these indications. This is because the originator trastuzumab has gone through the whole process of clinical development, and the biosimilar has proven to have the same mechanism of action, safety and efficacy profile as the originator.¹⁰

Speak to your doctor

Interaction and collaboration between patients, nurses, doctors and other medical staff, are essential elements for the successful use of biosimilars in cancer treatment.

It is your right to be informed about any treatment you receive. If you have any questions or concerns about biosimilars or other treatments, you should ask your doctor.



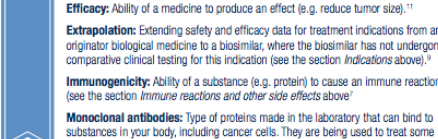
Frequently used terms you may want to know

Efficacy: Ability of a medicine to produce an effect (e.g. reduce tumor size).¹¹

Extrapolation: Extending safety and efficacy data for treatment indications from an originator biological medicine to a biosimilar, where the biosimilar has not undergone comparative clinical testing for this indication (see the section Indications above).⁹

Immunogenicity: Ability of a substance (e.g. protein) to cause an immune reaction (see the section Immune reactions and other side effects above)

Monoclonal antibodies: Type of proteins made in the laboratory that can bind to substances in your body, including cancer cells. They are being used to treat some types of cancer.¹²





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 similar are there?

-The rise of biosimilars

-Are biosimilars the future in oncology/haematology?

2004

2008

2018/9

- Barriers to the use..
- The challenge of...
- Paving the way for...

The End of Phase 3 Clinical Trials in Biosimilars development?

Requirements for an application without an efficacy trial

Prerequisites for the reference product

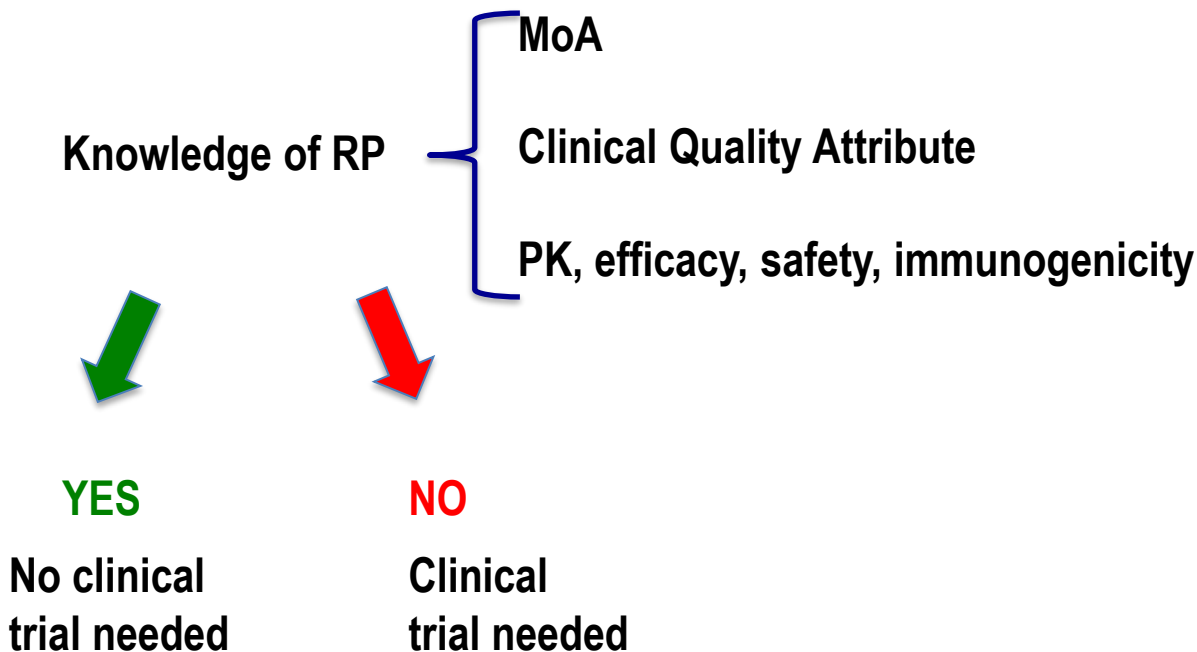
Biosimilar development starts with in-depth knowledge of the RP. Its main and potential secondary MOAs in the target diseases need to be known and demonstrable. As a result, the physicochemical and functional properties that are more likely to relate to the clinical outcomes will be identified, which 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.



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

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HOW TO BUILD → HOW TO CONSOLIDATE CONFIDENCE

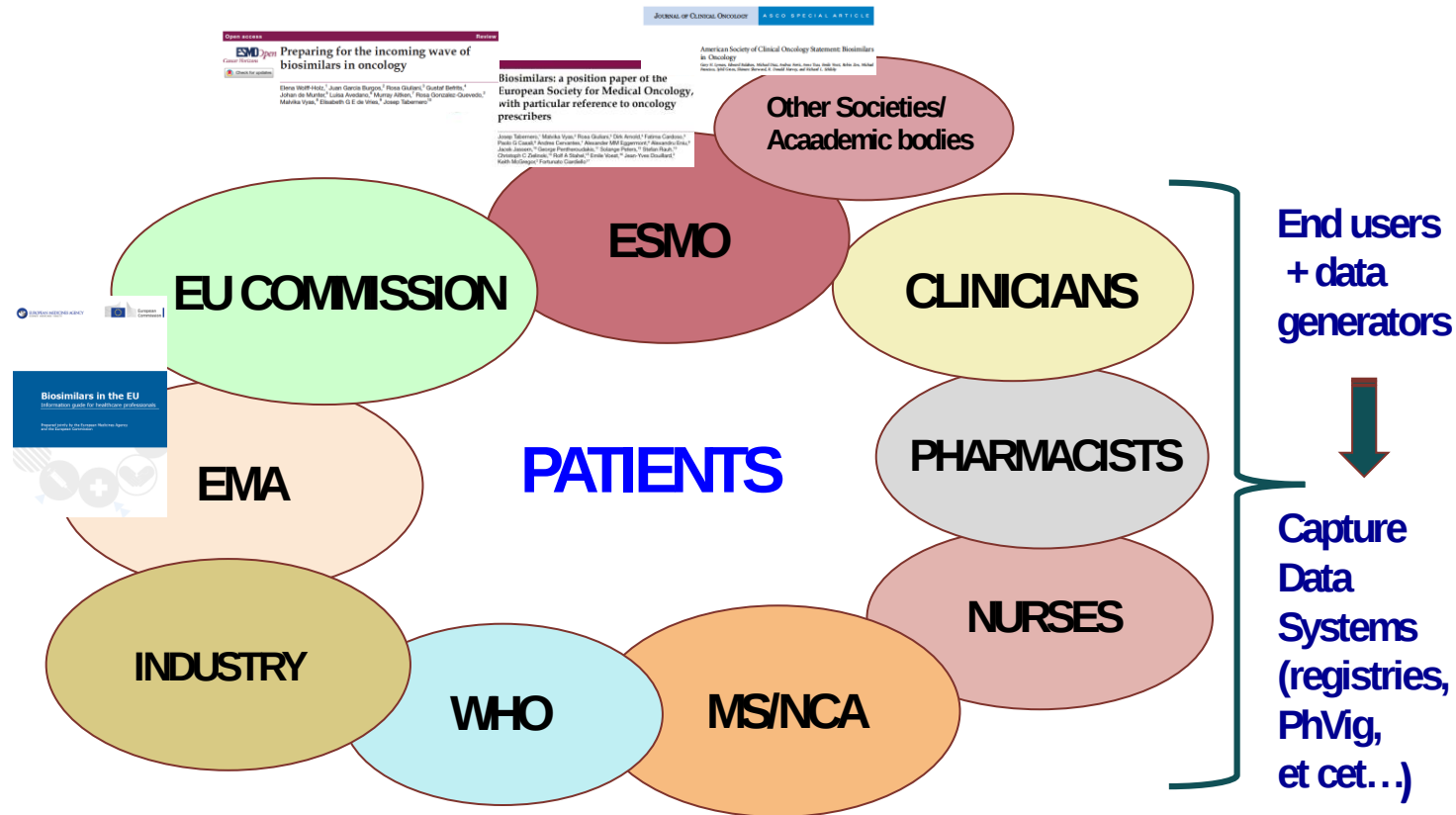
SCIENCE

GUIDANCE

INTERACTION/
COLLABORATION

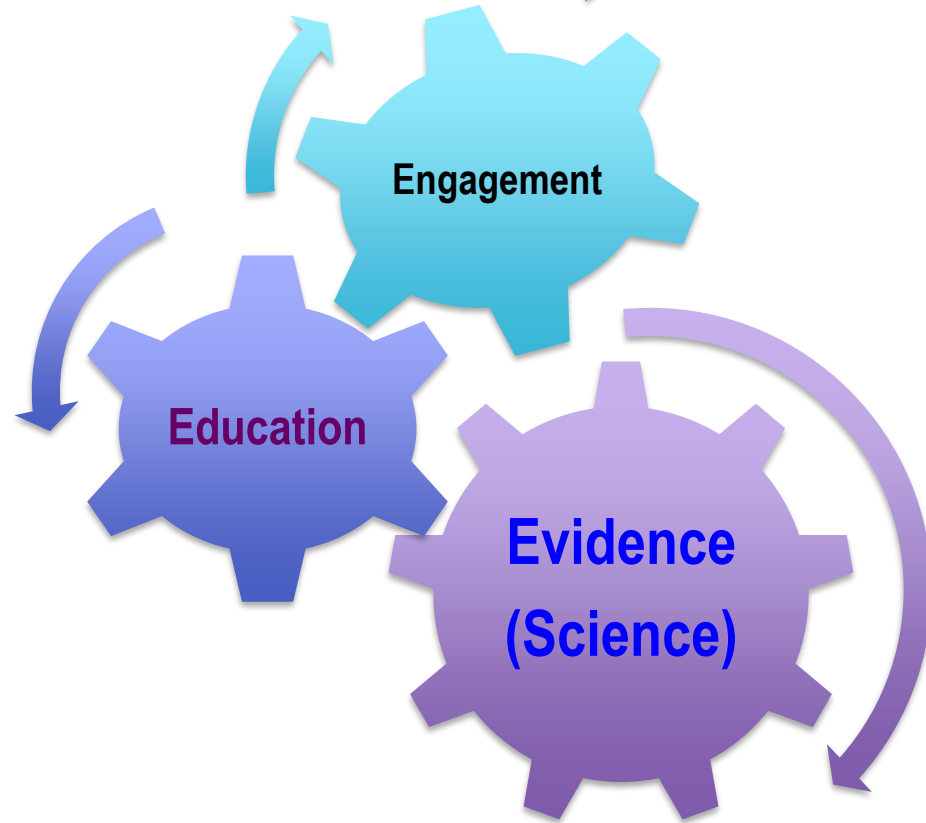
DATA COLLECTION

DATA ANALYSIS



SUCCESSFUL IMPLEMENTATION

SCIENCE





Confidence



SCIENCE

REGULATORY EXPERTISE